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ANTHONY HARRISON

GETTING THE RIGHT MEDICINES?

Putting public interests at the heart of health-related research

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ANTHONY HARRISON

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Anthony Harrison is a visiting fellow at the King's Fund. He is the author of numerous studies in health care policy, including a critique of publicly funded research, *Public Interest, Private Decisions: Health-related research in the UK*, published by the King's Fund in 2002.

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Preface

Since the Second World War a large and commercially powerful pharmaceutical industry has developed in the United Kingdom, which successive governments – in the name of economic growth – have supported through fiscal and other incentives. Thanks to massive spending worldwide on health-related research, this industry has developed a range of new drugs for combating disease and disability.

Few would contest the benefits these developments have brought about in terms of improved health. However, the current system in the United Kingdom largely reflects the interests of providers, including the producers of pharmaceutical and other health products, and those working in research establishments. In recent years there has been a growing recognition within the health field that provider interests do not necessarily or consistently coincide with the requirements of users of the health care system. In some situations the interests of providers may in fact prevail over those of users; in other cases user needs may not be addressed at all.

This discussion paper, *Getting the Right Medicines?*, contributes to our understanding of these issues with specific reference to research in pharmaceuticals. It focuses on the system for investing in the research and development of new interventions in health, and tests whether it always works in the public interest.

The King's Fund works to improve health and health care. To this end we often use our independent resources to support those individuals or groups who find it hard to make their voices heard in policy debates. We are also concerned to ensure that government policy can demonstrate that it addresses the health needs of all sectors of society. *Getting the Right Medicines?* is a contribution to the debate about how to further the influence of those who are currently marginalised in the pharmaceuticals research process, namely the users of the existing health care system.

Anthony Harrison

Summary

An implicit public–private partnership for the UK pharmaceutical industry

The UK Government has been at the forefront of developing public–private partnerships (PPPs). These partnerships are based on the view that neither public ownership nor privatisation is the only answer to the provision of public services, but that a partnership between both sectors can exploit the strengths of each.

Since its establishment the NHS has had close links with the pharmaceutical industry. Although there has been no formal PPP there has, in effect, been an implicit public–private partnership for the provision of pharmaceuticals (that is, medicinal drugs). The pharmaceuticals industry and government interact and work together in a number of important ways, from early blue-skies research that might throw up new ways of developing drugs, through to the final stage when decisions are made about the use of drugs within the NHS.

This implicit PPP involves the following main elements:

- **Research and development (R&D)** The private sector is the main spender on R&D for pharmaceuticals although the public sector offers support through subsidies or tax breaks to the industry and also carries out and funds medical research on its own account.

- **Patents** The pharmaceutical industry is bound by the patent laws applicable to all branches of enterprise. Patents offer protection from competition, which creates the conditions within which profits can be made. These profits finance the large scale R&D that drug development requires.

- **Access to NHS patients and facilities** The development of drugs from laboratory to actual application is dependent on the availability of NHS patients for trials of the drugs. Pharmaceutical companies also need to use physicians and researchers, many of whom will be NHS employees, to carry out the trials.

- **Medicines control** State regulatory bodies determine what drugs can be sold and under what conditions – in the United Kingdom these are the Committee on the Safety of Medicines, the Medicines and Healthcare Products Regulatory Agency and the National Institute for Clinical Excellence (NICE).

- **Price control** In the United Kingdom, as in most other developed countries, prices are controlled through a voluntary agreement known as the Pharmaceutical Price Regulation Scheme (PPRS). This is deliberately designed to leave companies an adequate profit margin to finance a high level of research, at the cost of increased prices to the NHS.

- **Scientific and clinical professions** These groups work within the public and private sectors but they are also to some degree autonomous, operating under rules of their own.

The implicit partnership has been strengthened and made more explicit through the work of the Pharmaceutical Industry Competitiveness Task Force (PICTF). This task force, set up in 2000 and jointly chaired by a minister and a senior industry figure, has identified a number of ways in which the Government can improve the process of drug development and in so doing help maintain a strong pharmaceutical industry in the United Kingdom.

Has the implicit PPP delivered?

Within the existing implicit PPP the pharmaceutical industry has been the active driver, largely free to provide products that it considers likely to be profitable. The Government has tended to be a passive purchaser, rarely proactive and only in limited instances making clear requirements for specific outputs.

Given this, it is no surprise that the implicit PPP has been an economic success. For example, in 2001, the value of UK pharmaceutical exports was over £9 billion, with a record trade surplus of some £2.9 billion.

However, there are two significant problems with the way in which the implicit PPP currently operates:

First, because it is focused on new medicinal drugs, the implicit PPP neglects some other research areas that may be potentially beneficial for promoting people's health, such as alternative therapies. Research designed to protect and promote health currently attracts far fewer resources than research focused on the search for new pharmaceuticals.

Second, the implicit PPP does not fully take the needs of some major groups, including women, children and older people, into account. The Government has introduced a number of initiatives designed to empower patients and the public in the governance and delivery of health care. However, these reforms have not yet been extended to pharmaceuticals research.

There are weaknesses with each element of the implicit PPP. More importantly, the partnership as a whole is not sufficiently focused on achieving better health for the UK population. A reshaping of the framework within which the implicit PPP operates is needed if users of the health care system are to get a better deal.

Widening the implicit PPP

The current implicit PPP needs to be widened to include citizens and service users more effectively in decision-making, and to undertake research into areas of potential health benefit other than new forms of drugs treatment.

To promote these outcomes the roles of the private sector, public sector, the scientific and clinical professions and health service users need to be reworked. Changes by sector include:

- **Private sector** Incentives for the private sector have to be re-examined and modified in favour of ones that can be better used to promote publicly chosen objectives. This is likely

to involve experimentation with elements of the implicit PPP (*see* p vii for description), such as alternatives to patents.

- **Public sector** The Department of Health is unclear about where the current health research economy is failing. To address this it requires a greater strategic capacity. The benefits of expanding the public role also needs examining in the areas of basic research, pre-competitive research, neglected therapeutic areas, care delivery, and clinical research and trials in areas that attract no commercial funding. The independence of the whole process must be guaranteed, with more public oversight. The regulatory role should be modified to ensure openness, absence of bias, high scientific standards, and the promotion of trials that promise the greatest health gains.

- **Scientific professions** Further measures should be taken to ensure the science underlying the development of drugs and other therapies is independent.

- **Citizens and service users** Health service users are being encouraged to take a more active role in their own care and there are moves to involve members of the public – as citizens and service users in the running of the NHS. These developments suggest that users should also be formal partners in any revised PPP for pharmaceutical provision. The broader involvement of citizens could lead potentially to a radical reordering of research priorities and possibly encourage research into areas such as low-risk drugs, self-administered treatments, non-invasive interventions and measures which avoid the need for treatment.

Recommendations

While economic success is clearly a legitimate objective for a UK government to pursue, so too is the health of the nation. An implicit PPP focused on health-oriented research and development would be based on the following key principles:

- ☑ There should be systematic evaluation of neglected areas of research and development where there is potential high benefit, whether in the development of new drugs or therapies, or in areas such as post-licensing clinical trials.

- ☑ There should be equality of opportunity (in research terms) for different therapeutic options.

- ☑ All parts of the drug (therapy) development process should be considered at one and the same time.

- ☑ Citizens and service users should have a voice at all stages of the research process.

- ☑ It has already been identified that some groups are neglected or poorly served by existing research and development programmes in the public and private sectors. There is therefore a case for a Health Research and Development (R&D) Task Force. This task force could set about systematically identifying all the areas poorly served by the current implicit PPP and identify the appropriate response on behalf of the Government, the rest of the public sector and the private sector.

This Health R&D Task Force should be established according to the following guiding principles:

- The task force itself should not directly involve any research providers. It should only include users of research such as clinicians and other decision-makers, and current and potential users of health services.
- Taking into account the principle above, its membership should be diverse in terms of disciplines and fields of expertise as well as personal experience.
- It should be able to commission research in its own right into the priorities of citizens and service users, and into the current balance of research effort between new forms of treatment and other types of health care.
- It should operate on a continuing basis.
- It must be seen to be independent and therefore its operations need to be completely transparent.

Specific issues the R&D Health Task Force might consider include:

- how the public sector could be a better purchaser by developing the role of NICE 'upstream' and ensuring that the earlier stages in the therapy development process produce the data it needs
- the gaps in the health research economy
- the economic advantages of alternatives to patents, which preserve incentives to drug development within the private sector
- how to redesign the process of defining the need for clinical trials so as to create a level playing field between trials that are driven by commercial interests and those undertaken for socially beneficial reasons
- how the process as a whole – not simply the individual parts – can be improved.

The recommendations set out above are intended to lead to the development of a public–private partnership (PPP) for the promotion of health. What the proposed Health R&D Task Force would in fact recommend remains an open question but it is likely that, at least in some respects, its proposals would conflict with the private sector's view of its own interests as creators of employment and other benefits to the UK economy. The Department of Health would therefore be faced with the tricky problem of how to put together the results of the work done by the proposed Health R&D Task Force and that of the Pharmaceutical Industry Competitiveness Task Force (PICTF).

It has to be recognised that if the department were to attempt this task it would face a fundamental difficulty: regulation of the pharmaceutical industry is an international enterprise and so there are limits to what one country can achieve on its own, particularly if, like the United Kingdom, that country has a substantial industry. But while this presents an obstacle to some possible policies, such as a substantial change in the licensing regime, it does not get in the way of others, such as a redirection or expansion of the funds currently devoted to health-related research.

Moreover, in this field, a greater degree of internationalisation would be a positive factor since all developed countries share similar problems around such issues as adherence to drug regimes and control of their drugs spending. The recent report from the G10 (European Commission 2003) is an example of the scope for joint work. This report identifies a number of areas for international action but some, such as the creation of incentives to encourage research in line with public health priorities, can also be tackled at national level.

The Department of Health has recently restructured itself so as to focus on the strategic issues that only it can tackle. The task of getting the best – from the health viewpoint – out of the UK pharmaceutical industry and the wider health research economy is surely one such issue.

Ways forward

The King's Fund is ready to support the establishment of a Health R&D Task Force, if others express an interest in its development. For this task force to be effective it must include the views of all those who may be poorly served by the existing arrangements. This means, primarily, the general public, who are current and/or future users of health care. It also means clinicians and public health experts who may challenge the focus of research programmes on new treatment as opposed to the effective application of existing interventions, or highlight bias towards commercially viable interventions over other approaches such as behavioural change or public health measures.

On a wider front, the King's Fund remains committed to improving health for all – and to challenging the inequalities faced by particular groups in society. Our activities include:

- **Promoting greater public and patient involvement in health and health care issues** – as a route to greater ownership of health and health issues at individual and community level, and to more responsive and inclusive services.

- **Drawing attention to areas where public interests, or the needs of particular communities, are under-represented** – such as the health-related research discussed in this paper, or the case for investing in local health 'advocates' in some of London's most deprived areas, to act as a bridge between health care professionals and their communities' needs.

- **Helping develop an effective health system** – with a greater focus on health outcomes, not simply on service delivery. In 2004, we launch a broad programme of work looking at how a complete 'health system' might work – for example, by building stronger leadership at national, regional and local levels, or by developing local health organisations that help people safeguard and improve their health throughout their lives.

1 An implicit public–private partnership

This section introduces the concept of public–private partnership (PPP). It describes the implicit PPP that exists between the pharmaceutical industry and the Government, and identifies the main organisations involved. It argues that the current partnership is built on the assumption that what is good for the pharmaceutical industry is necessarily good for health promotion, and it sets out how this assumption will be analysed in the rest of the paper.

Public and private roles in pharmaceutical provision

From the establishment of the NHS onwards, links between the pharmaceutical industry and the NHS have been close. In effect there has been an implicit but not precisely defined public–private partnership (PPP) between the industry on the one hand and the NHS and the Government on the other. The latter has been represented principally by the Department of Health (and its predecessors) and the departments responsible for funding research and higher education.[1]

WHAT IS A PUBLIC–PRIVATE PARTNERSHIP?

Public–private partnerships (PPPs) cover a range of relationships between government and the private sector including:

- introduction of private-sector ownership into state-owned business using the full range of possible financial structures such as different ways of sharing ownership
- long-term contracts for the supply of services, for example, hospital buildings and their maintenance, again through a variety of contractual forms
- using private expertise to sell government services into a wider market or to exploit the market potential of government assets , for example the transfer of intellectual capital from government research establishments.

PPPs are based on the view that neither public ownership nor privatisation is the only answer to the provision of public services. What is best has to be worked out on a case-by-case basis; there is no set formula.

Within health, the Government has successfully promoted the use of private finance in the provision of hospitals and is currently actively promoting partnerships with the private sector in the provision of elective care and other services.

In 2000, the Government moved to make the implicit PPP explicit through the establishment of the Pharmaceutical Industry Competitiveness Task Force (PICTF – *see* 'Key organisations in the implicit PPP' on p 3) 'to retain and strengthen the competitiveness of the UK business environment for the innovative pharmaceutical industry' (Department of Health 2001b, p 16). Announcing the establishment of the task force, the prime minister stated that 'A key feature in maintaining the United Kingdom's attractiveness will be effective partnership at the highest levels between Government and industry.' (*see* www.doh.gov.uk/pictf)

Subsequently, in its *Science and Innovation Strategy*, the Department of Health indicated that 'measures to improve the competitiveness of the pharmaceutical and other healthcare industries' form a key underpinning of its broader aim of ensuring 'that science and innovation lead to improved interventions for health and social care' (Department of Health 2001a, paras 1.5, 1.3).

The Department's role in this partnership (para 2.3) involves:

> *... helping ensure that the industry has an environment in which it can flourish to benefit the nation's health and wealth. Working in partnership with industry is increasingly important in harnessing the benefits of new technologies for health and quality of life... The department has a major role to play in ensuring that the UK remains an attractive base for industry.*

There are several areas of interaction or partnership between the industry and the NHS which the department claims benefit both the companies and the NHS (Department of Health 2002a). One such area is clinical trials. These, the department notes, help the UK industry to be a world leader, while the NHS benefits from the medicines developed as a result. Another is the development of national service frameworks for major diseases and need groups. The Department of Health's website indicates that 'the Secretary of State is keen to involve the pharmaceutical industry in the development of national service frameworks' (*see* the 'National Service Frameworks' section at: www.doh.gov.uk). The website goes on to set out the various stages at which such involvement might take place within each framework, including initial development, membership of the external reference groups which steer them, review of emerging findings and practical implementation.

Does wealth equal health?

The department's implicit assumption in both these examples is that measures to support wealth creation through its sponsorship of the industry also support health creation, and that a partnership designed for the one purpose is equally relevant to the other. In other words, what is good for the UK pharmaceutical industry is good for UK health. The final report of the PICTF (Department of Health 2001b, para 1.11) states that:

> *... the Government needs to ensure that in supporting a vibrant and profitable pharmaceutical industry it also supports a vibrant, modern, high-quality National Health Service (NHS). The NHS is very largely funded directly by the UK taxpayer rather than through public and private health insurance funds, as is the case in many other advanced economies. Providing an efficient and effective NHS costs money – expenditure on medicines consistently forming a rising element of overall costs. However, there is no doubt that good health, and the part medicines play in providing it, are important factors in generating a vibrant UK economy. A healthy economy in turn – of which a successful pharmaceutical industry is an important part – will provide the resources to deliver a world class health service in this country.*

KEY ORGANISATIONS IN THE IMPLICIT PPP

NICE – the **National Institute for Clinical Excellence** – was established in 1999 as a special health authority within the NHS. Its main role is to provide guidance to patients and professionals on good practice. It undertakes assessments of the efficacy and cost-effectiveness of individual drugs, and develops clinical guidelines for use within the NHS, based on systematic reviews of all the available clinical and economic evidence.

The **Pharmaceutical Industry Competitiveness Task Force (PICTF)** was established in 2000 and its final report issued in 2001. Its terms of reference required it to bring together the expertise of industry leaders in the United Kingdom with government policy-makers to identify and report to the prime minister on the steps that may need to be taken to retain and strengthen the competitiveness of the UK business environment for an innovative pharmaceutical industry. Progress on implementing the task force recommendations is described in the subsequent report, *One Year On* (Department of Health 2002b)

The **Medicines Control Agency** – now merged with the Medical Devices Agency to form the **Medicines and Healthcare Products Regulatory Agency (MHRA)** – has been charged since 1989 with protecting public health by ensuring the safety, quality and efficacy of the medicines on sale in the UK. Its key role is the granting of licences to sell drugs, whether prescription-only or otherwise, but it also has an inspection role in relation to drug manufacture and distribution, and in the surveillance of drugs once they are in use to detect any undesirable side effects.

The **Medical Research Council (MRC)** is the oldest UK research council. It supports research in universities and other institutions and also has major research facilities of its own. It is the public-sector supporter of clinical trials and carries out or finances blue-skies research including new scientific areas such as genomics. A concordat between the MRC and the NHS, designed to encourage the MRC to take account of the needs of health care services and public health measures, has been in place for over a decade.

The report recognises that a balance has to be struck between supporting the NHS and the industry, but no tension is acknowledged between the two aims: essentially they are seen as being in harmony. The PICTF's *Clinical Research Report* (Department of Health 2001b, p 5)[2] confirms this:

> *There has been a long tradition of pharmaceutical industry interaction with the NHS, to the benefit of both parties, patients, and the competitiveness of the UK generally in biomedical sciences.*

There is, however, no reason why the interests of the industry and the NHS (and its patients) should be identical. For a coincidence of interests to exist, two main conditions must be satisfied:

- First, that the incentives facing the industry (created by the pursuit of profit) lead it to seek out those therapeutic options likely to create maximum health return for UK citizens.
- Second, that where this is not so, mechanisms such as direct public funding or other forms of intervention can be relied upon to fill the resultant gaps or modify the incentives facing the industry so as to align public and private interests.

This discussion paper argues that neither condition fully holds. The incentives facing the industry are such that some areas of potentially valuable research are neglected. However, the public side of the implicit public–private partnership is neither adequately resourced to fill the resulting gaps in research nor capable of other forms of response to the existence of neglected opportunities for promoting health. The result is a lower level of health benefits than could be obtained if the PPP were properly designed and the roles of both public and private sectors more carefully defined. The aim of this paper is to identify what needs to be done to make the existing implicit PPP more effective in health terms.

2 The implicit PPP in outline

This section introduces each of the elements that make up the implicit public–private partnership (PPP) in pharmaceutical provision. It also examines the implicit PPP as a whole from two perspectives: as an economic arrangement and as a contributor to health.

Elements of the implicit PPP

The main elements of the implicit PPP are set out in the box below. In all the areas identified, both public and private sectors make a contribution to the development of drugs and other therapies, but the relationship between the two 'sides' varies widely between the different elements.

The remainder of this section will provide a brief overview and critique of each element of the implicit PPP, and of the implicit PPP as a whole. Section 3 will consider in detail how the elements identified below can be modified to improve health outcomes.

Research and development (R&D)

Most drugs are derived directly or indirectly from scientific research. The public role here has been acknowledged since 1917 when the Medical Research Council (MRC) was established.[3] Since then there has been a well-recognised division between pure or blue-skies research carried out by the public sector and more applied research undertaken by private companies.

Patents

The extent of private commitment to research depends on the availability of patents and the terms on which they are made available. Therefore the role of the private sector is critically dependent on the state using the powers uniquely available to it to grant patents.[4]

Access to NHS patients and facilities

As drugs come towards the stage of clinical application, the nature of the PPP changes: once a promising entity is developed, further progress towards the marketplace is entirely dependent on the health care system making available patients for trials and clinicians for managing them. This division of roles does not stem from differences between the public and private sector but rather from the nature of their respective functions. In other countries where there is a larger private health care sector, the public sector may not be involved at this stage, or at least not as a care provider.

In other words, the partnership at this point is between the industry and the health care system, rather than between the industry and the public sector. Nevertheless, precisely

because the NHS does form part of the UK public sector and comes under the control of a department of government,[5] this area of interaction must form part of any public–private partnership.

Medicines control

The final stage of drug development stretches the notion of partnership to the limit as it involves the statutory regulation of the industry's products and, potentially, refusal to allow them to be marketed or used within the NHS. The public role derives from the need to balance the interests of producers on one hand and consumers and taxpayers on the other. In principle, the industry might self-regulate and avoid state control. But following the thalidomide disaster, the UK Government brought in the 1968 Medicines Act, which created the existing regulatory machine comprising the Committee on Safety of Medicines and the Medicines Control Agency (MCA);[6] other countries took similar measures.

From the industry's viewpoint, the public sector's regulatory role is the source of massively increased commercial risk; from the perspective of the public sector, this stage is vital to ensuring that the industry's products promote the outcomes that it seeks and, with the addition of the National Institute for Clinical Excellence (NICE) to the regulatory regime, that they are cost-effective as well. Not surprisingly, the regulatory process is the site of conflict rather than partnership.

Price control

The price of drugs once they enter the market is another source of tension between the partners. The payer's wish for low prices conflicts with the desire of the industry for profits, although the payer may take the long view that profits are the source of finance for research into new drugs. This role is acknowledged within the Pharmaceutical Price Regulation Scheme (PPRS) which, in one form or another, has been in operation for most of the life of the NHS. While curbing drugs prices, it also explicitly allows ample profit margins in the expectation that this will allow the industry's substantial research programmes to continue.

In principle, this tension over price could be eliminated by the public sector taking over the drug development process. However, the implicit PPP rests on the assumption that the incentive built in by the profit motive creates a vehicle for drug development which the public sector cannot match.[7] If this is correct then price regulation coupled with the patent regime must be designed to preserve this incentive.

Scientific and clinical professions

The rules imposed by the public sector on private companies are not the only ones bearing on the way the implicit PPP works. To a degree, the science on which drug development rests is a self-governing entity, imposing its rules on whichever sector it is employed by: its integrity rests on the presumption that the results of the scientific work, including testing with patients, are based on sound scientific methods and reported honestly. The same is true of the medical profession. Hence both could be regarded as a third party to the implicit PPP, trusted to carry out their roles without intervention from government.

However, this trust has been abused in ways that have undermined the apparent integrity and independence of science from, in particular, the interests of the private sector. Accordingly, new rules imposed by government and others are beginning to enter the implicit PPP in an

attempt to ensure that science works in the way that it should,[8] whether it is carried out in the private or the public sector.

The medical profession (and to a lesser extent other clinical professions) is also part of the implicit PPP. The integrity of medicine – in its role as guardian of the patient's interests – has also been threatened in recent years by commercial pressures that, where they have been strong enough, have in effect hijacked its authority to the benefit of one of the private partners in the implicit PPP. Here too, measures are being introduced by the professions themselves as well as government to counteract these developments.

Putting the elements together

A key principle of PPPs is that the paying partner should be able to define what it wants in broad enough terms to allow the provider scope for determining how to produce it (*see* 'What is a public–private partnership?' on p 1). One Treasury paper states, for example, that within PPPs, 'Government retains the responsibility and democratic accountability for deciding between objectives' and 'defining the chosen objectives' (HM Treasury 2000, para 4). But having specified the objectives it wants to promote (the output specification) and determined the balance between them, the Government does not attempt to define how the chosen objectives should be met – that is left to the private partner.

In a broad sense the implicit PPP for pharmaceuticals follows this pattern. The paying partner (in the United Kingdom, this is the Treasury via the NHS) wants drugs to deal with the illnesses it treats. But only in a few areas such as immunisation and vaccination, where specific needs can be defined, is the output specification more precise than this.

It follows that the active driver in the partnership is the industry and the profits it seeks to make. The public role is enabling – through its support for research and provision of access to patients – and responsive: it regulates the entry of new products to the market and influences their price but it does not attempt to define the products themselves. Hence the public role is not, with some exceptions, proactive.

In brief, the implicit PPP is a permissive framework. It is not designed to produce drugs serving specific therapeutic goals but rather to make a profit-based drug development process viable in a manner consistent with other goals such as safety and, to a lesser degree, economy, on the assumption that this process will generate health benefits for the NHS and its patients.

But as the citations throughout Section 1 clearly showed, the implicit PPP also serves another objective: the economic and financial success of the UK pharmaceutical (and biotechnology) industry. The permissive framework serves this objective well, as it leaves the industry free to develop those products which it considers likely to be successful in international as well as national markets. This is not to say that the implicit PPP offers everything the industry wants.

The Pharmaceutical Industry Competitiveness Task Force (PICTF) was established to address the concerns of the industry about issues such as the cost of carrying out clinical trials within the NHS that hindered its overall performance (*see* 'Key organisations in the implicit PPP' on p 3). In effect, the task force report and the resulting activities represent a move from the informal interaction that has typified relationships between industry, government and the NHS, to a partnership in which the participants' roles and responsibilities are more carefully designed.

An economic success

In economic terms, the implicit (although increasingly explicit) PPP is a success. The UK pharmaceutical industry remains, despite the existence of price control, a major exporter, employer and investor. The following figures, taken from the *Pharmaceutical Price Regulation Scheme: Sixth report to Parliament* (Department of Health 2002c, p 15), support this:

- The pharmaceutical industry employs nearly 65,000 people directly in the United Kingdom with several times that number employed in related activities.
- The industry invested over £3 billion in R&D in 2001. This investment represents some 25 per cent of the United Kingdom's total manufacturing industry expenditure on R&D.
- In 2001, the value of exports was over £9 billion, with a record trade surplus of some £2.9 billion.
- Alliances between the industry and universities have increased dramatically in recent years with companies funding collaborative research programmes with universities to the value of £70 million.
- R&D in the pharmaceutical sector has benefited to the tune of some £500 million from the extension of R&D tax credits to large companies.
- The UK biotechnology sector accounts for 62 per cent of products in late-stage clinical trials in Europe.

The Department of Health estimates the net value of the pharmaceutical industry to the UK to be some £700–2,000 million, plus a terms of trade effect of £1,000–2,000 million (*see* website at: www.doh.gov.uk/pictf/value.htm). Drug prices are lower than they would be in the absence of the UK industry.[9]

These data suggest that the economic objectives of the implicit PPP are being successfully promoted; they will not be considered further here. From this point on, the focus of this discussion paper is solely on the success or otherwise of the implicit PPP in furthering the health objective.

Assessing the health benefits of the implicit PPP

There is extensive evidence of the success of the worldwide pharmaceutical industry in promoting health. A series of studies by Lichtenberg (1999, 2001, 2002a, 2002b) found that the introduction of newer drugs as a result of pharmaceutical innovation resulted in a reduction in overall medical costs, an improvement in workforce participation and an extended life span. Another survey (Neumann *et al* 2000) identified a wide range of effective science-based interventions including drugs. Other studies offer support both for individual drugs or for their contribution to reducing the impact of particular diseases.[10] As the United Kingdom is a major player at world level and directly responsible for some of the pharmaceutical innovation included in these surveys, the evidence suggests that the implicit PPP is successful in health as well as economic terms.[11]

But could it work more effectively than it does now? If we start from the position of the NHS as a purchaser and of its users as consumers of drugs, is it possible to redefine the implicit

PPP so that it works better from the health point of view? Answering these questions requires an examination of the role of both the private and the public sectors and the nature of their interaction. The essence of a PPP, implicit or explicit, is that the roles of all the partners must be properly defined so that they mesh together and complement each other. Gaps or failings may stem from a failure to define the respective roles of the partners as much as from individual weaknesses. This holds both for the individual elements listed on pp 5–7 and for the process of drugs development as a whole.

Furthering health outcomes through the implicit PPP

Ultimately in any PPP it is the purchaser who must determine whether or not the PPP is working, given the objectives it is trying to promote. In this paper we are assessing what needs to be done by government and the NHS if the health objective is to be more effectively promoted. Before doing so we need to consider this objective in more detail.

The evidence cited above from the work of Lichtenberg and others suggests that the implicit PPP is producing benefits to the users of the resulting products in terms of longer life and a reduction in illness and disability. While these are the central goals of any health policy, the purchaser of the output of the implicit PPP has other requirements, principally effective clinical and economic decision-making. For these requirements to be met, knowledge is required, not simply of the therapeutic benefits of a new drug, but also how its performance compares with others and the cost of achieving those benefits. For clinicians making day-to-day decisions as to how to treat their patients, relative performance is critical. For those charged with setting limits to the use of resources within the health care sector – in the United Kingdom, the National Institute for Clinical Excellence (NICE) in particular – both types of information are critical. The process of drug development as a whole must therefore be designed to meet these requirements.

3 The elements of the implicit PPP

This section analyses key elements of the implicit public–private partnership (PPP): research and development (R&D), patents, access to NHS patients, medicines control, price control, and the scientific and clinical professions – with specific reference to how each of them contributes to health. It also looks at how effectively the elements of the implicit PPP interact as a whole.

Each element of the implicit PPP involves some form of interaction between the public and the private sectors. This section considers whether the 'terms of engagement' within each element work well or whether, through modification or complete redesign, they could be made to work better from the health point of view.

Research and development (R&D)

The health research economy in the United Kingdom is dominated by the private sector, but the public and the private not-for-profit sectors also make substantial contributions (*see* Table 1). The public contribution takes two main forms: first, spending within public research institutions including universities and second, financial support for private-sector spending.

TABLE 1: SPENDING ON HEALTH-RELATED R&D – THE MAIN PLAYERS (2000)

Research funder	Amount (£ in millions)
Private, for profit	3,000
Private, not for profit	540
Department of Health	500
Medical Research Council	300
Higher Education Funding Council for England	190

Source: King's Fund

Note: The data in this table are not strictly comparable: they do not refer precisely to the same time period and they are collected on different bases, but they reflect the broad picture.

Public spending on research

Although all new drugs could be said, in a broad sense, to be underpinned by science, the process of finding an entity which works, and does so without significant side effects, is essentially hit or miss with many more misses than hits. This is true at all stages of the process, from basic research through to the final stage of clinical trials. It is an expensive, risky process and hence inherently unattractive to the private sector. This case was accepted

in HM Treasury's *Cross Cutting Review of Science and Research* (2002, para 50), which argued that:

> *Basic research is highly speculative and long term in nature. Many avenues of research will prove unfruitful while huge wealth-generating potential (for example) can occur unexpectedly. It is therefore unlikely that industry, left to itself, will fund this form of research.*

The initial stage of pure, fundamental or blue-skies research might be characterised as the most risky stage of drug development. By its nature such research is some way from potential application and in some cases may be regarded as speculative or, even worse, theoretical. Although it would be wrong to characterise all publicly funded medical science as 'pure' or unrelated to immediate applications, the majority falls into this broad category. How much is spent in this high-risk area cannot be established from the available data, but the role of the Medical Research Council (MRC) and, to a lesser extent, the other research councils and the higher education funding councils largely corresponds to this view of what the Government should be doing or financing.[12]

This division between pure and applied research, although not clear cut, has been one of the elements of the implicit PPP for nearly 100 years – the public sector paying for long-term, speculative or basic research into, for example, understanding the functioning of cells, and the private sector exploiting this work as a source of insights as to where resources should be deployed to meet specific therapeutic goals. The origins of many drugs and medical devices can be traced to research funded from the public purse and often carried out within the public domain.[13]

This contribution is particularly appropriate for public funding where there is little chance of patents being granted. As Eisenberg (1996, p 1,726) has put it:

> *Public funding may... be justified under a public goods rationale if the character of the research is such that patentable outcomes are likely to be the exception rather than the rule and the research promises substantial social benefits that cannot be captured by patent holders.*

The public and private sectors may also interact to the benefit of each on a continuing basis. According to Cockburn and Henderson (1996, p 12,730):

> *The ability to 'do good science' in the private sector may not be supportable in the long run without a close partnership with the institutions of open science. Policies which weaken these institutions, make public sector researchers more market-oriented, or redistribute rents through efforts to increase the appropriability of public research through restrictions in the ways in which public and private sectors work with each other may therefore be counterproductive in the long run.*

Furthermore, making the knowledge gained from research freely available, and hence not profitable to obtain, prevents unnecessary duplication of effort. The free exchange of knowledge is essential to the development of science as a whole since the value of one piece of knowledge may be vastly increased when it is combined with others. Commercialisation of public-sector research (which is current government policy) may reduce the effectiveness of this process.

This exchange process may also be imperfect because the incentives promoting the necessary exchanges are limited and the process itself is expensive. Hence there may be a public role in dissemination. As the Department of Trade and Industry white paper, *Excellence and Opportunity* (2000a, para 33), puts it:

> *... there are often market failures in the networks and links which bring the public and private researchers and industries together. Although all parties would benefit from these linkages being stronger, it is in no one party's interest to take on the cost and responsibility for forming these networks. That is why public funding can play such a critical role. Government can facilitate such links to help turn scientific ideas into innovation. This means examining new public–private partnerships to bring businesses and universities, ideas and finance closer together, as well as initiatives to create regional clusters. Government cannot and should not attempt to manage these networks but it can play a critical role in facilitating their creation.*

This citation suggests that the role of publicly funded research is not simply to provide knowledge that commercial interests can then use to develop new products, but also to improve the exchange of knowledge and provide a source of expertise throughout this process. Cockburn and Henderson (1996, p 12,725) found that:

> *... public sector research plays an important role in the discovery of new drugs, but [that] the reality of the interaction between the public and private sectors is much more complex than a simple basic/applied dichotomy would suggest. While in general the public sector does focus more attention on the discovery of basic physiological and biomechanical mechanisms, the private sector also invests heavily in such basic research, viewing it as fundamental to the maintenance of a productive research effort. Public and private sector scientists meet as scientific equals, solve problems together, and regard each other as scientific peers, which is reflected in extensive co-authoring of research papers between the public and private sectors.*

The division between public and private is therefore not absolute. Part of the value of the public role lies in its availability as a source of expertise, not simply as the source of particular pieces of knowledge. Such expertise may be drawn on during the process of drug development by scientists working within the industry. These scientists may themselves produce research findings that are made publicly available through the normal processes of scientific publication.

Nevertheless the broad division of roles remains valid, as does the general presumption t that publicly funded work will be (freely) available. This is not generally the case for research funded by the private sector, since knowledge gained privately must generally be kept private and/or patented so as to provide the incentive for the required commitment of resources later in the development process.

While the current broad division of roles may be justified, however, it is less clear whether the current balance between public and private sectors is appropriate. Even if the public good and other arguments for public spending on research are accepted, it is hard to determine what represents an appropriate level of commitment and, in particular, whether the current level of public spending is correct.

The UK programmes have not, as a whole, been subject to outside scrutiny since 1988,[14] and there has been very little public discussion about their scale or purpose. In 2002 the Medical

Research Council (MRC) published *A Vision for the Future: Consultation document,* which it described as 'an exercise in thinking ahead about how scientific opportunities and health needs might develop over the next decade'. It does not address even indirectly the question of funding or, even in broad terms, the productivity of the research it is planning. However, as the Science and Industry Committee of the House of Commons noted (2003) in its report on the MRC, the council is rejecting alpha-rated projects (that is, projects that in its view should certainly be funded). This would seem to be *prima facie* evidence that extra funding could be put to effective use within the public sector.[15]

This finding did not lead the committee to a more wide-ranging consideration of the case for promoting a significant expansion of public-sector research, either to improve the productivity of the health research economy as a whole or to meet the needs of the NHS. Such an omission reflects a more general failure of the UK public-sector component of the health research economy. The current public-sector spending on health-related research is not underpinned by an explicit consideration of what the public sector as such should be doing. The Department of Health R&D website continues to stress areas of national priority – more or less the national service frameworks – without explicitly at least considering what it is that publicly funded research should be addressing. Consideration of that must start with an assessment of where the private sector currently fails to carry out research and where it would continue to fail to do so even if the incentive structure was altered.[16] As things stand, the current public-sector role in research can be justified by the general arguments set out above, but the harder question of how much should be spent on what remains unanswered.

Financial support

Public support for pharmaceutical R&D is also offered through fiscal incentives or subsidies. The pharmaceutical industry benefits more than most because of its high R&D spending. The critical issue here is the relationship between the returns on research enjoyed by the industry and those experienced by society as a whole. The general case for subsidising research through fiscal means rests on the view, supported by extensive research, that the social returns to R&D are greater than the private – in other words, the private companies carrying out research cannot capture all its benefits. In the case of drugs, for example, there is evidence that they can produce considerable benefits in areas not originally targeted when they were developed (Pritchard 2001).

But there are reasons for arguing that private returns may overstate social returns. When the House of Commons Health Committee examined the relationship between the government and the industry it concluded that some R&D was designed to preserve commercial interests rather than promote new discoveries – in other words it identified a conflict between the two objectives of the implicit PPP. The committee recommended in 1994 that the Department of Health should monitor more closely the research for which the companies were claiming costs under the Pharmaceutical Price Regulation Scheme (PPRS) (House of Commons Health Committee 1994, conclusions para 14):

> *Research which is aimed at duplicating existing drugs within a therapeutic category in which sufficient products are already available, or which is simply disguised promotion, should be disallowed under the Scheme in order to divert funds to more pressing areas of research.*

This suggestion was firmly rejected by the then Government (Department of Health 1994, p 7):

> *The Government does not accept the committee's suggestion that there should be Government interference in or direction of the research programmes of the pharmaceutical industry. There is no evidence that these programmes are wasteful or unproductive. There is a competitive imperative for every company in such a research-based industry to get the best results, in terms of therapeutic advance, from the large sums it spends on them. The company's future in the world market (of which the United Kingdom accounts for only three per cent) depends on those results.*

This response fails to address the central criticism that the competitive imperative is not confined to the search for therapeutic advance but is also concerned with economic or industrial advantage. The committee's accusation is in fact supported by substantial evidence. Glennerster and Kremer (2000) argue that the present patent system and the rewards structure that flows from it 'create an incentive to design around the first patent so as to produce a competing vaccine and obtain a share of the market'.

According to these authors, 60 per cent of patented innovations are imitated within four years; as the average cost of an imitation is about two-thirds of the original, the result is a socially wasteful use of scientific talent. According to a report by the National Institute for Health Care Management in the United States (2000), the Food and Drug Agency (FDA) approved 1,035 new drugs between 1989 and 2000, two-thirds of which used active ingredients already on the market. The vast majority were not considered to offer any additional therapeutic benefit although the existence of competing drugs should result in lower prices.

A related charge is that the current level of R&D is not productive in therapeutic terms. Garattini and Bertele (2002) argue in relation to cancer drugs that those approved by the European Medicines Agency in recent years have shown little or no advantage over existing drugs, yet are typically much more expensive.[17] The work by Lichtenberg cited earlier, although not specific to cancer, is consistent with this finding as it suggests that 'pharmaceutical innovation... appears to be subject to the law of diminishing marginal productivity' (Lichtenberg 1999, p 29). His estimates of benefits in terms of reduced mortality for the 1980s were much lower than those for the previous decade.

Not surprisingly, therefore, Taylor (2003, p 408) has concluded that there is a 'crisis in productivity in pharmaceutical research'. It is also apparent from the financial performance of the large international companies that they are struggling to find new products.[18] A recent survey of the state of the industry cites the director of the European Agency for the Evaluation of Medicinal Products as saying: 'Never has so much money been spent on research and development with so little result' (Horton 2003, p 37).[19]

Evidence such as this does not by itself destroy the case for fiscal incentives to drug development, but it is sufficient to suggest that the case cannot be taken for granted. In particular, while the case may in the past have been very strong it is now less persuasive given the evidence of declining marginal productivity of research spending. We return to this point when we consider the PPRS (*see* 'Price control' on pp 25–26).

In summary, there is a strong case for a substantial commitment of public funds to pure or long-term research. This commitment is in line with the broad principle underlying PPPs that risks should be borne by the partner most able to do so. But beyond that, there is no explicit rationale for the current pattern of public spending – including subsidies for research – nor for

its scale. That can only come from an analysis of where current health research fails to perform well from the health viewpoint and where a public contribution can either lead to an increase in productivity in the private sector or an increase in spending in neglected areas. Without such an analysis the basis of the implicit PPP in respect of R&D is unsound.[20]

Patents

The industry enjoys the protection offered by the patent laws applicable to all branches of enterprise. The case for allowing patents is essentially the same as in other industries: it provides stimulus to investment in research.[21] However, in the case of drugs, the expense of development and the lengthy period over which resources have to be committed means that patents, or some other form of protection of intellectual property rights, are indispensable to the private sector's participation in the PPP.

In the case of so-called orphan drugs (those targeted on rare conditions) special conditions are typical. In 2000 the United Kingdom adopted the European Commission regulation designed to encourage the development of orphan drugs. The regulation embodies three incentives:

- the waiving of fees payable to the European Agency for the Evaluation of Medicinal Products (EMEA) as part of the process to obtain a Community authorisation
- guaranteed market exclusivity for ten years
- the setting up of a committee for orphan medicinal products within the EMEA which will provide expert advice on a range of issues.

(Department of Health 2000, p 2)

In addition the regulation provides for special incentives to R&D to be offered in this area.[22]

However, although patents generally have been regarded as the bedrock of the industry given its long lead times, their value is not as clear cut as it may seem. Essentially there are three lines of criticism:

- That the high prices that patents allow reduce the benefits of the drugs developed to the health care sector because they must be rationed if they are expensive or, if they are not rationed, because of their high opportunity costs (that is the benefits lost by not being able to spend on other drugs or treatments).

- That the creation of patents reduces the efficiency of the research process. Critical here is the way that innovation works. The simplest model is that a single major discovery leads to a single useable entity. In practice this is rare. As a result, the development of a new drug may involve the use of several patents and as a consequence the process becomes more difficult, more expensive and potentially open to 'blocking'.[23]

- That reliance on patents means that some potentially valuable topics are not researched at all.

The first of these criticisms is tackled in more detail later in this section (*see* 'Price control' on pp 25–26). The other two are explored further overleaf.

Patents and the research process

Heller and Eisenberg (1998, p 699), argue that the increasing use of patents may be damaging to the research process as a whole:

> *A proliferation of patents on individual fragments held by different owners seems inevitably to require costly future transactions to bundle licenses together before a firm can have an effective right to develop these products.*

This is just one of several criticisms of the way that patents work in practice. A review by Calandrillo (1998), drawing on a range of historical research into the impact of patents on innovation, identifies a number of ways in which they can be used to block rather than spur innovation. They can, for example, discourage the introduction of new products or processes where patenting of small improvements holds up more substantial ones. The historical record reveals many examples of this kind.

Cockburn and Henderson (1996, p 12,729) add to this argument by pointing out that 'public policy proposals which curtail the flow of knowledge between public and private firms in the name of preserving the appropriatability of public research may be counterproductive'. As we noted earlier they found that the current PPP involved a free flow of information between public and private sectors which it may be assumed was beneficial to both sectors and to the overall drug development process.

Cockburn and Henderson put forward their conclusion tentatively and it may well be that the risk is more of a threat than an actuality. However, it is a risk that current policy appears to ignore even as a possibility. If the over-privatisation of knowledge is a threat rather than a major obstacle, it is a threat which is likely to grow more rather than less important since in the United Kingdom, as in the United States, a major thrust of Government policy is to encourage the privatisation of publicly funded knowledge in the name of promoting enterprise.[24]

However, the problem identified by Heller and Eisenberg (1998, p 699) is endemic in the way that patents are used in the private sector. They argue there is a dilemma here:

> *Like the transition to free markets in post-socialist economies, the privatisation of bio-medical research offers both promises and risks. It promises to spur private investment but risks creating a tragedy of the anticommons through a proliferation of fragmented and overlapping intellectual property rights.*

As we point out later (*see* 'Private-sector role' on pp 29–31), others have argued that there are ways of offering rewards to innovation which do not have these side effects. If feasible, these alternatives would reduce the force of the dilemma but there is as yet only limited experience of their value in practice. Therefore the only conclusion to be drawn at this stage is that, while patents may be indispensable within the existing implicit PPP, the incentives they offer are not all benign: they offer opportunities to block progress as well as to encourage it. Accordingly, it cannot be taken for granted that they represent the most efficient means possible of providing incentives for drug development.

Lack of research outside of potential patent areas

A reliance on patents means that some potentially valuable topics are not researched at all. This critique is, as things stand, the most important. While the patent can be an effective

device, it is also a limiting one because it discourages research in those areas it does not encompass. This is essentially the problem for developing countries concerning neglected diseases.[25] In developed economies, the issues include:

- no incentive to research existing entities such as generic or out-of-patent drugs or natural entities used by alternative therapies
- an inherent bias away from therapeutic options other than drugs such as behavioural therapies which cannot yield a patent and from regimes which combine drugs and therapies of this kind.

In the developed world the market is not structured in such a way that all health care needs and different therapeutic treatments are equally attractive to the industry (or to firms which produce or might produce competing therapeutic options).

We now briefly review a number of areas of market failure in relation to patents: the exclusion of certain population groups, the extended use of drugs already in use but out-of-patent, natural drugs and alternative therapies, and treatments other than drug therapies.

Exclusion of certain population groups

Some major population groups are under-represented in clinical trials and the search for new drugs: women, children and the elderly. In the case of children, the House of Commons Health Committee report (1997, p x) into children's health concluded that 'the current situation in regard to the testing and licensing of medicines for use by children is unacceptable. Indeed, we were astonished to discover that this situation existed, and we imagine most members of the public would share our reaction'. The committee went on to note that off-label use (that is, use by patients of a drug for a purpose other than that for which a licence had been obtained) was not necessarily harmful and the Medicines Control Agency (MCA) gave assurances to that effect.[26] But they went on to add that: 'It is surely wrong that clinicians dealing with children should be put in the position, as they now frequently are, of having to guess what an appropriate dosage or route of administration might be.'

Similarly, a study carried out in The Netherlands found that drug labelling was often imprecise (for example, on defining the age of a child) and that a substantial number – over one-fifth – of prescriptions for children were used off-label, suggesting the potential for misuse was considerable.[27]

In respect of elderly people Yusuf (1999, p 566) writes that:

> *Many current trials have tended to underrepresent or even exclude older people... Elderly people usually have the worst prognosis and are also likely to be at the greatest risk of adverse events. Given that elderly people are the fastest growing segment of the population and that they have high rates of cardiovascular disease and related drug use, future trials should facilitate enrolment of large numbers of such patients.*

As Grundy (2002) points out, while recent trials of the effectiveness of statins have included older people, they were not designed to take account of the risk factors, including the use of other drugs which affect older people in particular. Many others have made essentially the same point.[28] Yet older people are by far the largest user group for medicines: they currently receive far more prescriptions per head than younger age groups and the rate of increase is also higher.

Extended use of drugs already in use but out-of-patent

A number of drugs have been found to be effective for conditions different to those for which they were originally developed. Although such discoveries are made, the incentives for this kind of research are weak. Garber and Romer (1996, p 14) point out that the discovery that aspirin can prevent heart attacks and death from heart attacks could not have been produced within what we have termed the implicit PPP:

> *It is difficult to conceive of realistic circumstances in which a producer of aspirin could gain exclusive rights to sell aspirin for this indication, and it is unlikely that the discovery that aspirin had such beneficial effects markedly increased the profits of its producers. Moreover, since aspirin is produced by many firms, no one of them had much to gain by financing this kind of research.*

They then go on to point out that developments of this kind may produce large benefits but small profits. Hence private funding is unlikely to be forthcoming and government-funded research may be particularly beneficial.[29]

Natural drugs and alternative therapies

The House of Lords Science and Technology Committee Inquiry into Complementary and Alternative Medicine (House of Lords 2000) found that there was little research into these therapies primarily because, unlike conventional drugs, the producers were small and not highly profitable. Although it expressed the hope that the industry would do more, it also oncluded that the Medical Research Council (MRC) and the NHS should pump prime the area with some dedicated funding – as the National Institute for Health has done in the United States. The Department of Health (2002d and 2003a) has responded with a very modest research programme: the sums involved are tiny relative to those deployed elsewhere in the health research economy. In the short term the supply side of both the provision of therapies and of related research is currently too weak to support a major programme, a fact that reflects the current incentives in both the commercial and the scientific world.

Treatments other than drug therapies

Evidence that drugs are effective in clinical and economic terms was presented in Section 2. The evaluations underlying these studies are essentially 'local', that is confined to the drugs and therapies concerned. The drug route to health improvement is well-resourced, but the potential of other routes is not systematically explored. These circumstances have produced health care systems that are highly drug dependent and that in general cannot see themselves being any different.

An earlier King's Fund study examined this failure of the health research economy (Harrison and New 2002). It concluded that, in large part, it is attributable to the failure of the public sector rather than the private sector to carry out or finance the research required to support improvements to the delivery of health care or the introduction of public health measures. In both areas publicly funded programmes exist, but they remain modest in scope.

This point has been brought out to striking effect by a recent review carried out for the Health Development Agency of public health interventions (Milward *et al* 2003). It found that only a tiny fraction of the publicly financed health research budget was devoted to public health interventions despite the fact that this has been recognised for at least 15 years as a priority

area.[30] It also applies to areas such as mental health where cognitive and other therapies are 'competitive' with drug regimes. The former attract very small amounts of funding in comparison to the latter. Similarly alternatives to the use of statins, such as dietary change, receive little research or service development support (Feinman 2003).

It appears that, from the industry's viewpoint, the patent is the greatest strength in the current implicit PPP. However, from the health viewpoint, almost total reliance on patents within the prevailing set of incentives is a significant weakness.

Patent protection cannot be abandoned because the process of drug development would grind to a halt. But other forms of incentive (*see* Section 4) are technically feasible. These alternatives could overcome some of the weaknesses of patents within the PPP as currently defined while retaining the current broad division of roles. However, in some cases it will prove hard to create alternative incentives structures and hence, if weaknesses of the types identified above are to be remedied, the public sector must take direct action through funding research in the private sector or carrying out its own research.

Access to patients

Despite the critical nature of this partnership element, there has been a lack of clarity as to the rules, financial or otherwise, under which access to patients should be allowed or encouraged. The industry's concerns were supported by the Pharmaceutical Industry Competitiveness Task Force (PICTF) which made it clear that this part of the PPP has not been working well. The task force recommended changes in current arrangements and steps have been taken to improve them. In March 2002 an R&D partnership agreement between the industry and the Department of Health was published. It was designed to ensure joint funding of clinical research and 'faster development of new drugs for patients' (Department of Health 2002a). In January 2003 the department published a model agreement (2003d) designed to promote research within the NHS but (largely) funded by the industry. The agreement was described as:

- setting the parameters for commercial contracts between NHS bodies and companies for commercial research
- enabling joint funding of trials which are of a non-commercial nature but which are important to both industry and the NHS
- providing for industry to contribute to research infrastructure in the NHS.

The announcement went on to note (p 3) that: 'There is global competition between countries for undertaking research for the pharmaceutical industry. The group's report... pointed to issues of timeliness/speed of starting trials, costs and quality of research as factors affecting this country's competitiveness' (Department of Health 2003d).

The draft agreement states starkly that the objective of establishing the Clinical Trials Working Group was 'to identify actions necessary to maintain and improve the international competitiveness of industry-sponsored clinical research in the UK' (*Ibid,* p 2).

But from the health viewpoint the critical issue is whether the trials being funded offer the greatest potential therapeutic benefit, including their contribution to clinical and economic decision-making. Because some trials may not be of direct commercial benefit, for example if they compare the cost and clinical effectiveness of different drugs and different combinations of drugs, they are unlikely to be the ones that the industry wishes to promote and hence a conflict may arise between economic and health objectives.[31]

Garattini and Liberati (2000, p 846) point out that for many medical problems there are several classes of pharmacological drugs with different mechanisms of action, but that we shall probably never know how they compare on efficacy and safety because 'there are clear economic reasons why no one is interested in investigating whether drug A is better than B, C or D'. The result is bias from omitted research.

Heidenreich and McClellan (2000, p 31) found this form of bias in the case of innovations in acute myocardial infarction (AMI) treatment:

> *... the marginal value of trials for treatments that are not under patent is relatively high. In the case of streptokinase, earlier funding of a large trial could have led to significantly more patients receiving thrombolytic drugs sooner.*

The UK Government does support a substantial trial programme. The MRC in particular has a significant programme and it recently published the results of a review of its portfolio (Medical Research Council 2003). Evidence offered to this review described gaps of the kind identified above. For example, the consultation carried out for the review asked what role the MRC should play in meeting national needs for clinical trials, and whether this role is distinct from that of other funders including industry, government, the NHS and charities. One response to the consultation preceding the review ran as follows (MRC 2003, p 17):

> *It should play a major role in funding those clinical trials which might bring greatest gain to the health and wellbeing of the UK population. The trials undertaken should be prioritised using a collaborative process between UK governments, the NHS and charities. The focus would be on those areas where industry is unlikely to have an interest but would bring great health gain.*

The industry representative made a similar point: 'The MRC should seek out gaps in clinical research that are not covered by the other three main funders... ' (*Ibid*, p 23).

The review itself argued for more trials of complex interventions such as those intended to change the behaviour of patients or practitioners. It also noted that the MRC is considering setting up a ring-fenced fund to help put such interventions on a more even footing with those involving drugs.

Although the review identified a number of weaknesses in the way that trials were currently supported, it did not address the wider questions of whether:

- sufficient resources are devoted to them nationally
- existing programmes produce the kind of results which the NHS needs for effective clinical decision-making, and which the National Institute for Clinical Excellence (NICE) requires to inform its role of arbiter of what drugs should be paid for by the NHS.

There is evidence that they do not. In the case of cancer it has become clear that, despite the importance of the disease and a number of research reviews in the 1990s, recruitment to trials has been poor. The implication is that the public sector has been unable to organise itself properly to carry them out, although measures are now in train to remedy this in the field of cancer.[32] We conclude that a policy for determining which clinical trials are likely to produce the most therapeutic benefit across the whole field of potential trials remains to be devised. That can only be achieved if the demand for trials reflects the health objectives rather than the economic objectives of the implicit PPP. Currently, however, the demand for trials reflects in large part the workings of medicines control.

Medicines control

In large measure the relationship between regulator and regulated is, at least at the surface, adversarial. The interest of the industry is to get drugs to market quickly while the interest of the regulator is to ensure that they are safe and effective. This may involve delays to give time for more evidence to be collected. Not surprisingly, the industry is not shy of complaining about the loss of benefits to patients if regulators are slow to give approval either for licensing or, as with NICE, for use within the NHS. Clearly a balance has to be struck which may at times seem wrong from the viewpoint of industry or drug user. But a number of substantial criticisms have been levied at the regulation process which suggest a fundamental imbalance between the interests of the industry and its users.

It is a cliché of the economics of regulation that the regulated industry eventually captures its regulator: Abraham and others have argued that this is the case in pharmaceuticals. As in other industries, regulation of pharmaceuticals was established so as to be entirely independent of the commercial interests of the companies. However, the recent review of NICE undertaken at its own request by a World Health Organisation team (Hill *et al* 2003) concluded that there was an inherent contradiction between the institute's key principle of transparency and the acceptance of material that is designated as confidential. It therefore concluded that the commitment of NICE to transparency and public accountability should override confidentiality issues and make it possible for decision-making to become more transparent and open to scrutiny.

According to Abraham (2002a, p 1,686) the regulatory bodies 'have been overly influenced by the industry's desire for rapid drug approvals'. In addition they (the various national bodies) are heavily dependent on the industry for their incomes and to some degree compete with each other. Furthermore, interchange of staff between regulators and the industry tends to promote similar sets of views.

This imbalance may show itself in egregious examples where the regulators have allowed through drugs which subsequently have had to be rapidly withdrawn.[33] However, more general and wide-ranging criticisms have been made about the secrecy of the process and, from some viewpoints, its lack of rigour and risk of bias. We shall now examine these in turn.

Secrecy

The regulators require information from the industry about the results of its trials. This information is usually treated as commercially confidential. Collier and Iheanacho (2002, p 1,408) argue that:

> *For the pharmaceutical industry investment in information is time and money well spent. However, the huge scale of work involved, a lack of openness, accompanying duplication, and distortion of the overall research effort and resulting messages makes the business of information-generation inefficient and threatens patient interest.*

The House of Commons Health Committee (2002) report on NICE found that the institute was not always able to access all information relevant to its decisions as there is no legal requirement for the companies to supply it. The committee therefore recommended that 'the Government should take steps to ensure the submission of all relevant clinical information to NICE', and hence for it to be made public. In contrast, the Medicines and Healthcare Products Regulatory Agency (MHRA) has full access but does not make the information it receives

public.[34] In its response to the committee the Government agreed that all relevant information should 'wherever possible' be made available for public scrutiny, but did not propose any new measures to ensure that it is (Department of Health 2002f).

Viewed from the health angle, these criticisms are substantial. Any health-oriented PPP would have to modify disclosure rules so as to ensure full revelation in all but the most exceptional circumstances. Cookson and Hutton (2003, p 176) argue that the benefits of greater disclosure are considerable:

> *The point of regulating the market for information is to enhance R&D competition, by facilitating product comparisons and allowing purchasers to make informed choices about which new products offer the best value for money. So long as there is transparency and accountability in the use of cost effectiveness evidence by purchasers, those firms capable of producing cost effective new health care producers will flourish, benefiting patients, taxpayers and shareholders alike.*

In other words, both public and private sectors should work better as a result of greater disclosure.

Lack of rigour

Abraham (2002a) uses the example of Halcion to argue that the current system lacks rigour. The focus of his argument is the relationship between licensing and post-marketing surveillance. His conclusion is that the latter is not carried out systematically enough and that 'a manufacturer's commitment to their product, albeit genuinely held, may conflict with a commitment to investigate thoroughly the dangers to public health implied by doctors spontaneous reporting about that product'. Abraham (2002a, p 1,684) goes on:

> *... the Halcion case suggests that manufacturers are unlikely to search effectively for compelling evidence against the safety of their drugs and, therefore, that a regulatory system which relies so extensively on industrial examination, is flawed.*

He points out (*Ibid*, p 1,686) that the regulators are subject to pressure which the companies are rich enough to exert:

> *... regulators' response to their own 'early warning systems' may be influenced by how they weigh up the importance of forthright patient protection against the threat to their credibility posed by potentially successful adversarial legal action by a powerful transnational company.*

Whether this is right or not, it is not clear that the balance between pre- and post-licensing research is correct. A recent editorial in *The Lancet* (2002, p 1435) pointed out that:

> *... all ADRs [Adverse Drug Reactions] are a vital part of the overall picture of a drug that pharmaceutical companies should present to doctors, patients, and regulatory authorities... Patients, doctors, and pharmaceutical companies might all be better served if companies were obliged to fund rigorous, protocol-driven post-marketing surveillance, and pay for these data to be analysed by experts independent of the company.*

In its report on the Medicines Control Agency (MCA), the National Audit Office (2003) also concluded that there were weaknesses in the post-licensing system. While the number of

withdrawals was low – 12 out of over 2,000 medicines licensed over a period of a year – the agency carried out a large number of regulatory actions at this stage on safety grounds (*see* Table 2).[35]

TABLE 2: REGULATORY ACTIONS OTHER THAN WITHDRAWAL OF A MARKETING AUTHORISATION

Type of action	Number of actions 2001/02
Variations to marketing authorisations	515
Automatic addition of drugs to the list of intensively monitored medicines	78
Articles on drug safety sent to all practitioners	26
'Dear doctor' letters	9

Source: National Audit Office 2003

The Department of Health has recently recognised that the yellow card regime, wherein doctors and other health professionals report side effects of drugs which have already been approved, needs to be improved. It has therefore proposed that individuals as well as professionals may report such side effects through NHS Direct (Department of Health 2003b). It will be some time before it becomes clear how effective this new arrangement is in practice.

If this is successful it would open up possibilities of reform of the kind proposed by Jones (2001) that, in effect, make the trialling process a collaborative one between all the interested parties. He argues for a revised process that would not only require complete openness about the data resulting from early stage trials but the abolition of stage 3 and 4 trials in favour of better post-marketing surveillance.

He also proposes that there should be scope for varying the approval regime according to the drug in question and a lengthening of the partnership arrangement involving an improvement to post-approval monitoring. Whatever the specific merits of these proposals, they serve to highlight substantive questions about current regulatory requirements and the balance between pre- and post-licensing research.

Risk of bias

At one end of the scale there are specific regulatory failures which can only be put down to the regulator placing too much weight on the interests of the industry. One such case arose over the licensing of Lotronix, described by Horton (2000) as a 'fatal erosion of integrity'.

This appears to be an extreme example of the industry offering poor information about its products and the regulator accepting it. However, more generally, it is not easy to define what constitutes a biased relationship when there are inherent conflicts of interest. The evidence offered by Abraham (2002b) on reductions in approval times can be read as being beneficial to both 'sides' given that users and industry have an interest in these times being shortened, provided the drugs concerned are safe and beneficial. Furthermore, there is an inherent tension between over-caution, which entails the risk of benefits of new drugs being delayed, and rapid approval and resulting disbenefits from inappropriate use. Jones's proposal cited above represents an attempt to find a more effective way of striking this balance.

Abraham's demonstration of the industry's widening influence rests on an assessment of procedures rather than evidence that drugs were wrongly approved. Most of the changes made to the regulatory regime have been sought and promoted by the industry and by obvious implication serve its interests.

This in itself does not mean they do not also serve the interests of users. However, in another study, Abraham (1998, p 49) concludes that:

> *While British regulatory authorities have provided doctors with no assessments of the carcinogenicity studies... on approving the drugs (non steroidal anti-inflammatory)... [they] have permitted results from animal studies that show the drugs in a positive light to be publicised to doctors. This is strongly suggestive of permissive regulation that has awarded the benefit of the specific doubt to industrial interests rather than to patients' best interests.*

In a later study, Abraham (2002b, p 1,167) cites a number of instances where the regulatory process favours the industry. Reviewing the past 20 years he concludes that 'the independence of drug regulation in Europe from the interests of the pharmaceutical industry has been severely threatened'. This view was given some support in a National Audit Office report (2003, para 4.16), which found that:

> *Stakeholders from the consumer and patient groups we consulted were concerned that the relationship between the agency and the industry it regulates may be too close. This perception is reinforced by the fact that the agency is fully funded by fees from industry, which is not the case in some other countries.*

However, while the report notes that there are potential conflicts of interest in practice, it does not suggest any changes to the existing regime.

Overall

The National Audit Office does not give much support to the view that the regulatory process has been captured although it acknowledges the risk. Drawing on evidence of the kind cited in this and the previous section, Gale (2001, p 1,870) characterises the existing system as expensive and wasteful. Its 'purpose is rational but the process is not and has unintended consequences'. He draws the broader conclusion that:

> *... the public interest is not well served by the current system of drug development. Independent scientific evaluation is the only route to safe, rational, cost-effective prescribing, and this route is blocked while regulatory studies are irrelevant to clinical need, while companies control access to relevant data, and while marketing considerations dominate the clinical development programme.*

Furthermore, as Maynard and McDaid (2003) point out, the clinical trials conducted for the purposes of medicines control rarely include economic variables. But these are essential if NICE and similar bodies are to work effectively in their role of assessing whether the NHS should purchase new drugs as they come on to the market. Furthermore, if Cookson and Hutton are correct, the lack of such data in the public domain means that market processes themselves do not work as well as they might since they discourage effective competition and innovation.

It follows that medicines control does not play its appropriate part within the implicit PPP if the interests of all the elements in the implicit PPP are taken into account. In particular, the NHS interests as a cash-limited service provider are given little weight. While the MCA has largely succeeded in ensuring medicines are safe, the process over which it presides requires redesign in the interests of the health objective of the implicit PPP.

Price control

The reliance of health systems on the products of publicly created monopolies based on patents has naturally led to some form of price control. In the United Kingdom moves to reduce the costs to the NHS of the industry's products date back to the 1950s when the first voluntary agreement on pricing was reached between government and industry (the PPRS).

The impact of this agreement was assessed in the 1960s by a committee under Lord Sainsbury. It concluded (Ministry of Health 1967, para 178) that:

> *... there were great obstacles to price competition and that the price regulation schemes of the Ministry had serious weaknesses. As a result, we have concluded that the existing conditions under which medicines are supplied to the National Health Service are not such as always to secure that prices and profits are reasonable.*

Nevertheless, the nature of the agreement remained substantially the same and it was not until nearly 30 years later that it was reassessed: in 1994 the House of Commons Health Committee (Summary para 6) concluded that the scheme worked reasonably well but:

> *The secrecy which surrounds the PPRS makes it very difficult for parliament, health care professionals or the public at large to know what the overall effect of the scheme is; and in particular, whether the balance which the scheme was created to achieve, between the interests of the industry and those of the NHS, is being fairly struck, or whether there is a pronounced tilting in one direction or the other.*

The Government accepted this argument and instituted an annual report on the workings of the PPRS that was designed to make it more transparent. In fact, although these reports do contain relevant information, for example on the cost of drugs in the United Kingdom relative to those of other countries, they do not reveal how the scheme works in terms of its influence on the industry and the incremental changes it brings about in the industry's economic and therapeutic performance. Accordingly, it does not in itself allow a judgement to be reached on the balance between the interests of the NHS (lower prices and greater health benefits) and the interests of the industry.[36]

Given the nature of the implicit PPP it is essential that the cost of new drugs is high enough to recoup R&D and marketing expenditures. But this high cost reduces the social value of the new drugs both directly, because their use may have to be restricted, and indirectly because of the opportunity costs of using them against the loss of therapeutic benefit in other fields.[37] Guell and Fischbaum (1995) argue that the use of price controls does have some short-term benefits through reducing this effect, but they cite evidence from a study by the US General Accounting Office (1994) which suggests that price controls tend to produce lower levels of R&D spending. However, in their view the disbenefits of control are impossible to measure since they involve hypothetical calculations of the value of lost research.[38]

Lawton (1999) remarks that the government claims for substantial savings to the NHS from the then most recent negotiation of the PPRS were specious: the 'savings' may simply result in higher future costs. But such a calculus has not, apparently, formed part of the department's thinking. Until it is, the merits of the PPRS and price control in general will remain unknown.

The 1999 revision of the PPRS introduced changes designed to put more emphasis on innovation than price control. It also indicated that the potential for further deregulation of price and profit controls would be considered. Would this be feasible?

There may be a case for ending the present scheme and allowing competition and more informed purchasing to take its place, as Lawton (1999) has proposed. Our overall argument suggests that any such change should form part of an overhaul of all the elements of the implicit PPP. Without that, how can we conclude whether the existing level of research within the UK pharmaceutical industry is worth paying for through higher prices to the NHS or not. And while it may have been worth paying for in the past, the decline in research productivity noted by Taylor and others raises the question of whether this continues to be the case.

Scientific and clinical professions

Modern health services and the authority of those who provide them are underpinned by decades of research, from basic science through to clinical application. This research has been to a large extent autonomous in two senses. First, the way it proceeds – that is, what counts as good scientific practice – has been largely dictated by those practising it. Second, although government and others have been instrumental in both funding research and supporting particular lines of investigation, in general clinical research has defined most of its own goals. Increasingly that is no longer true: the private sector has come to take a commanding position in the way that science is applied to therapeutic goals.

This growing influence can be seen in the relative sizes of the research budgets commanded by the private, public and not-for-profit sectors. The grip of the industry on the scientific community has become increasingly recognised as a danger to its independence and to the capacity of Government to take an independent view of the value of the implicit PPP. A number of studies have reported that published results are biased towards the interests of their sponsors and that results may be suppressed if they are unfavourable. For example Friedburg *et al* (1999, p 1,455) found that there was:

> *... a significant association between authors' stated qualitative conclusions regarding the costs and cost-effectiveness of these drugs and study sponsorship by the drug's manufacturers. Studies funded by the pharmaceutical companies were nearly eight times less likely to reach unfavourable qualitative conclusions than non-profit-funded studies and 1.4 times more likely to reach favourable qualitative conclusions.*

Similarly, a review of studies reporting biomedical research (Bekelman *et al* 2003) found a statistically significant association between industry sponsorship and pro-industry conclusions.

Another study (Stern and Simes 1997) found delay to be a significant biasing factor. Negative results tend to be published with a greater delay with the consequent risk that systematic reviews of the evidence available at one point in time may work on a sample biased towards positive results. A similar effect was identified in a review of the way that clinical trials are reported in the major journals (Nuovo *et al* 2002). Nearly all report relative (to placebo) risk reduction, which is likely to be the most favourable statistic, rather than absolute reduction and the number required to treat. A related bias was found by Kjaergard and Als-Nielsen (2002) who examined 159 trial results published in the *British Medical Journal* from 1997 and 2001: they found that the declaration of financial interest was associated with results favouring experimental interventions. Lexchin *et al* (2003, abstract) also concluded that 'systematic bias favours products which are made by the company funding the research'.[39]

A number of medical publications have attempted to redress bias resulting (or appearing to result) from commercial sponsorship by requiring authors to reveal their financial or other relevant interests. The editor of *Nature* (Campbell 2001, p 751) referred to evidence consistent with the fact that:

> *... although, in principle, science may be objective and its findings independent of other interests, scientists can be imperfect and subjective. There are circumstances in which selection of evidence, interpretation of results or emphasis of presentation might be inadvertently or even deliberately biased by a researcher's other interests.*

These 'imperfections' can also arise at institutional level. A report from the Association of American Medical Colleges (2002, p 1) points to the wider risks of this situation and points out that 'the growing perception that research institutions may have financial conflicts of interest also threatens to weaken public support for research'.

Similar concerns about science in general have been expressed in recent UK official papers. If science is not a trusted partner, the whole enterprise is at the risk of collapse through loss of credibility.[40] This stage has not yet been reached, but its prospect suggests that all parties to the implicit PPP have a common interest in taking steps to ensure that trust is maintained. This may require a conscious 'disentangling' of the scientific process from commercial processes through measures designed to ensure that the integrity and independence of science are both maintained and seen to be maintained.[41] One route to this has already been mentioned: a greater volume of independent and hence publicly funded trials. There should also be greater openness of all trial results.[42] Other measures may also be appropriate: these could include a greater role for publicly funded and conducted research combined with a reduced reliance on patent protection.

Such measures would bite primarily on the private sector. But the public sector is also at risk. The BSE crisis and the continuing debate over the safety of the MMR vaccine have undermined the credibility of public science among significant sections of the population. Transparency is a key requirement and the Government has already taken a number of steps to ensure that the scientific advice it receives is open to public view.[43]

Even so, more fundamental measures may be required to counter the inherent bias of the scientific community towards 'interesting' topics instead of those deemed to have greatest importance by the ultimate users of research, that is, the consumers of health services. What form these might take is discussed in Section 4.

The implicit PPP as a whole

The argument set out above suggests that the implicit PPP does not work in the health interest as well as it might. Each element has weaknesses, but the more important point is that the system as a whole does not serve the health objective effectively.

Many of the faults of the system have been laid at the door of the pharmaceutical industry by some highly vociferous critics. Our conclusion is different. Clearly the industry can be said to be at fault if it hides data unfavourable to it or if it undermines the objective processes of science. However, where the implicit PPP fails because the overall incentive and regulatory structure is wrong, or because publicly funded programmes do not compensate for failures in the private sector, then fault must be found elsewhere.

Our analysis has suggested that the central weakness of the implicit PPP is that the public partner has not been an informed purchaser. Instead it has been largely content to have its output specification – which has been vague, indeed largely unexpressed – interpreted for it by the private sector. The main casualty of this has been that the search for therapeutic options, including public health interventions that cannot be patented, has been under-financed. So too has the search for the best among existing options where competing treatments exist.

This line of argument has been widely accepted within the very active debate about the contribution of the industry to the health problems of developing countries, (*see*, for example, Kettler and Towse 2003). In recognition of this, the World Bank has been active in promoting PPPs in this field precisely because market forces within the existing framework will not adequately meet the interests of these countries.

The argument in this paper rests on the view that essentially the same issues arise within the developed world. Although the nature of the market failure is different, the solutions will also involve a reshaping of the wider framework within which market processes work.

In response to this, we recommend a new form of PPP that will offer a continuing incentive to drug development while also ensuring the health care system gets a better deal. How this might be done is considered next.

4 Widening the public–private partnership

This section considers how the implicit public–private partnership (PPP) might be widened to include users and respond to a broader agenda that promotes health rather than just providing drug treatments. It re-examines and reworks the roles of the main players that are involved – the private sector, the public sector, and the scientific and clinical professions – and suggests how user involvement could be introduced to the partnership.

This section considers how the implicit PPP might be improved by considering in turn the roles of the main actors within it. So far the analysis has focused mainly on the role of private industry, government and science as a partner in its own right. In doing so the role of the ultimate users of drugs – patients – has been omitted. Implicitly the assumption has been that government and the NHS act on their behalf. In the rest of the NHS and indeed throughout the public sector, that assumption is no longer tenable. Formal and informal mechanisms are in place to allow the user voice to be heard directly and they are slowly being introduced into the research field. Accordingly, any modification of the implicit PPP would have to involve users in their own right, in particular to ensure that those whose voices are weak within the existing implicit PPP have an opportunity to make themselves heard.

The rest of this section considers therefore how the roles of the existing participants in the implicit PPP – private sector, public sector and the scientific and clinical professions – should be modified in the light of the conclusions of the previous section, and what role users can and should play in it.

Private-sector role

The analysis so far has shown that if the implicit PPP is to work better in the health interest then the incentive structure for the private sector – principally the patent – has to be modified in favour of incentives which can be better used to promote publicly rather than privately chosen objectives. The groundwork for doing this is in the process of being laid but is far from complete.

In a classic review of the economics of invention incentives, Wright (1983, p 691) argues that:

> *Though public intervention in the market for research is virtually universal, economists have paid surprisingly little attention to the choice of the form of research incentive in a given market structure. Many studies concentrate on patents, but any assumption of their superiority over other incentives has been founded on intuition rather than formal analysis.*

In recent years this gap has begun to be filled. A series of studies have examined alternative mechanisms. These include:

- **Patent-buyouts** Guell and Fischbaum (1995) propose that the Government buy prescription drug patents at a price equalising the net present value of the profit they would have generated and make these available to US drug manufacturers. They recognise that it would be difficult to determine a scheme that achieved this but nevertheless believe it would be feasible to do so.

- **Commitment to purchase** A number of organisations and individuals have proposed schemes of this kind particularly in the area of vaccines research. Kremer (2000a, 2000b) has reviewed the feasibility of a number of schemes of this kind. Clearly no commitment can be financially open-ended; equally it must be credible otherwise it would not act as an incentive to carry out research and development (R&D).

- **Prizes** The prize offered for the invention of a device which would enable ships at sea to measure the longitude of their position is the best-known example of this kind but they have also been used in recent times for commercial inventions.[44] Their potential has been promoted recently because they overcome many of the disadvantages of patents since the invention becomes a public good. According to Shavell and van Ypersele (2001) a system of rewards used in conjunction with patents works more effectively than either in isolation.[45]

- **Risk sharing** In 2002 the Department of Health announced that it had agreed with the suppliers of beta-interferon a form of risk-sharing that would allow the drug to be used to treat patients – which NICE had not found it possible to approve on the evidence offered to it – and payment for the drugs to be related to therapeutic success. The particular form of the agreement has been extensively criticised,[46] but this is a pioneering attempt to redefine the relationship and the balance of risk between public and private sectors and patients.

- **Cost-sharing** The Department of Trade and Industry operated a scheme during the 1990s known as Medlink (sometimes Medilink) that funded collaborative and pre-competitive research into new medical devices.[47] Project costs were shared between the companies and the Government. This form of support is particularly appropriate to smaller companies that do not have the capacity to fund substantial research from their own resources.

Although these mechanisms have clear merits on the level of principle and their potential value can, on various assumptions, be calculated, there is only limited experience of their use. Even their protagonists recognise the practical difficulties of implementation. Accordingly, even on the most optimistic assumption, they are best regarded as supplements to, rather than replacements of, the existing patent system, at least in the short term. The same is true of the potential of so-called open models of innovation that do not rely on patents at all (Butler 2003).[48]

If we were to start from scratch – but taking the experience of patents in practice – it is not obvious that patents would emerge as the best option given their negative as well as positive effects. However, we have to start from where we are and that means continuing and re-examining the existing patent regime. A revised implicit PPP should explicitly allow for experiment and innovation in rewards systems for both the private sector and those parts of the public sector (such as universities) that compete for funding. Their main role may be to act as a stimulus to work where the incentives created by the patent system do not operate

for the reasons set out above. In other words, they would be complementary rather than competitive regimes.

In making this suggestion, we are assuming that the private sector would largely remain responsible for most of the process of drug and other therapeutic development. However, it is possible to imagine a greater role for the public sector here. In fact the Government's proposals for exploiting public-sector intellectual capital tend to push in this direction by encouraging public-sector organisations including the NHS, the Medical Research Council (MRC) and the higher education sector to capitalise on the intellectual capital their research generates. In the short and medium term this role seems likely to be very limited.

We have also set out reasons why some elements of the existing development process should be moved from the private to the public sector in whole or in part. Our discussion of the weaknesses in the current regulatory regime, the gaps in clinical trials and the 'corruption' of science suggests that, even if the private sector continues to require and finance trials, the way it does so should be modified in such a way that the independence of the process is guaranteed. This would not necessarily mean a switch from private to public, but it would mean a much greater degree of public oversight.

Public-sector role

The main conclusion of our analysis is that the public side of the PPP has been weak. With the exception of vaccine development, the public sector has not attempted to define what specific outputs it is looking for nor has it attempted a systematic assessment of the performance of the health research economy – public and private – in relation to the health of UK citizens.

Harrison and New (2002) argue that the Department of Health plays a very limited role in the health research economy. Although it cannot direct it, since the main elements are largely autonomous or come under the aegis of other parts of government, it should be in a position to assess whether the current balance of effort serves the public interest.

The central weakness of the existing situation is the absence of a departmental view on where the current health research economy is failing and what should be done about it. The first requirement of the new PPP therefore is that the Department of Health develops this strategic capacity or ensures that it is developed elsewhere.

How much further its role should extend depends on the scope for modifying the way that the private sector operates. Put simply, the greater the scope for modifying the incentives bearing on the private sector, the smaller the direct public-sector role as a financier or provider of research needs to be.

In the short term, a major extension of the public provider role may not be effective or efficient. In a discussion of PPP in respect of the diseases of poverty, Kettler and Towse (2003, p 27) consider the 'public-sector only model' but conclude:

> *We are sceptical of the logic of the public-only model. The PPP model is designed to work with private industry in part because many of the background patents that researchers would need are in the hands of companies. In addition, the private sector possesses skills and resources that no one else has experience of or access to. For the public sector to seek to replicate all of these skills would be highly inefficient and time consuming.*

This pragmatic conclusion is hard to contest. If some part of the research carried out by the industry is, in health terms, wasteful, then one implication is that the process of drug development would be better carried out to a greater degree than it now is within the public sector. However, the public sector does not necessarily embody the right incentives either. As Glennerster and Kremer (2000, p 35) put it: 'The government often has difficulty in selecting appropriate research projects and in motivating researchers to focus on developing viable projects'.

Researchers have their own incentives which may not coincide with the interests of health. The glittering prizes of science do not necessarily lead in the direction most likely to promote therapeutic benefit, particularly if there is no clear view as to where that benefit is most likely to be found.[49] Furthermore, the pressure to maintain or increase budgets may lead those in charge of public-sector institutions to exaggerate the prospects of success from the lines of research they are pursuing in a manner analogous to the private sector promoting the merits of a particular drug. Moreover, the financial and other pressures bearing on universities, such as the research assessment exercise, may reduce their incentives to conduct some forms of health-related research.[50]

None of these points is strong enough to rule out some enlargement of the public role where the private sector is not strong or for other reasons unwilling to participate. Such a role is already apparent in respect of vaccine development. The Department of Health's Science and Innovation Strategy (2001a, para 2.16) states that: 'One area in which the Department of Health plays a very particular role in technology development and transfer is in vaccines development'.

It goes on to describe the way in which a vaccine programme was established involving various parts of the public sector and vaccine manufacturers once the department had identified the possibility that there would be an increase in Group C meningococcal disease. Five years after the need had been identified a national vaccine programme was in place.[51] Similarly, the apparent success of Medlink suggests that PPPs in pre-competitive research are also feasible and effective.

Our analysis suggests that the public role should expand, with or without a partnership with the private sector, in at least the following areas:

- **Basic research** The research councils and the higher education funding councils finance basic research but their budgets are tiny relative to the National Institutes of Health (NIH) in the United States. Accordingly, any expansion could only be justified by reference to the NHS interest.

- **Pre-competitive research** This is especially the case in economically weak sectors of the health research economy following the pattern of Medlink (and its successor).

- **Neglected therapeutic areas** The Department of Health has no programme targeted at neglected areas as such, but in 2002 it did establish a small fund for support of research into complementary and alternative medicines (CAMs), which was further extended in 2003.

- **Areas such as care delivery, which are complementary to the above** Some of these fall to the public sector now, but some straddle the interests of both public and private or could be made to do so if the financial structure was right. With drugs in particular there is

evidence of poor delivery, which greatly reduces what therapeutic value they have (*see*, for example, WHO 2003). In addition, however, there are well known gaps that bear on the way that care is organised and that promise high returns (Fulop *et al* 2003 and Department of Health 2002e).

- **Clinical research and clinical trials in areas that attract no commercial funding** This could be because they focus on comparisons between existing drugs or are too large for other sources of funding to support.

All the above imply an expansion of the public-sector R&D budget. Even in the relatively benign climate for public spending which now exists, the case would be hard to make. But essentially it would be the same as that made within the Pharmaceutical Price Regulation Scheme (PPRS) for protecting private research expenditure: the extra public-sector costs of this expansion would, in principle, be compensated for by lower treatment costs and health gains to NHS users. These savings have never been demonstrated within the PPRS and, in general, attempts to demonstrate the value of research in the United Kingdom have been limited to particular projects rather than broad programmes such as that of the MRC.[52] In principle, however, it would seem possible to make a 'business case' for extra public spending on health-related research at least as convincing as that put forward for other major health programmes not directly focused on patient care (such as the electronic patient record and the wider programme for introducing information technology to the NHS).

For several reasons, the public sector's regulatory role requires modification to ensure that:
- there is openness of the regulatory process, as recommended by the National Audit Office (2003)
- the results of the trials carried out to assess the value of new drugs are presented in an unbiased way and, of course, carried out in a way that meets high scientific standards
- the 'right' trials are done (those which promise the greatest health gains).

The aim of these measures should be to remove suspicion that the industry can manipulate the results of the work it is obliged to carry out, to ensure that when recommendations are made by the National Institute for Clinical Excellence (NICE) the work is presented with the appropriate evidence, and to use the trial process to the greatest benefit of clinicians and hence of patients.

Less clear is whether changes in the balance between pre- and post-licensing trials can be justified. As Jones accepted in response to criticisms of his proposals, the case for this rests on evidence that is not in the public domain. Its strength also varies with the nature of the drug in question and the practical scope for strengthening post-licensing surveillance. At present his suggestion seems more like a research than a policy proposal but if his surmise was demonstrated to be correct then policy changes should follow.

Role of the users

The implicit PPP is designed to promote and protect the interests of patients. All participants would 'sign up' to a mission statement of that kind. But our analysis has shown that, although it may generally work in that way, it does not inevitably do so. Furthermore, the user plays virtually no part in the PPP and hence has no influence on the way it works. We need therefore to consider whether the PPP as a whole could be modified so as to better reflect the user interest.

Clearly 'user interest' – like 'public interest' – cannot be defined in any simple way and the scope for user influence, given the technical nature of the drug development process, is inherently limited. There is no reason to believe that all users will have the same preferences; indeed, as far as treatment goes, the assumption underlying the process of informed choice and patient partnership is that they do not. It is well known that tolerance of drugs varies between people. Hence it is entirely rational to seek a range of interventions for any specific condition – as indeed the 'me-too' process does but at very high cost – and also forms of intervention other than drugs, which some may find more acceptable.

Nevertheless, there are general grounds for arguing that users should be formal partners in a revised PPP. The main reason is that, when they are given the opportunity, they do demonstrate that their views are different from professionals and that they can, albeit sometimes with help, engage with some of the technical issues. As Thornton (1999, p 724) puts it: 'We need to recognise that patients... have the experience and skills that complement those of researchers. They know what it feels like to suffer a particular disease and to undergo the treatments with their various side effects'.[53]

From the mid-1990s onwards attempts have been made to engage users in determining research priorities and in clinical trials. As far as 'process' is concerned, user representation on public-sector grant-giving bodies is limited, but possibly growing: the MRC report on clinical trials made significant recommendations in this respect. Many NHS as well as charitable trusts do engage consumers in their decision-making. Hanley *et al* (2001) report that out of 62 co-ordinating centres for clinical trials, 23 reported that consumers had been involved in their work.

Moreover, following the establishment of a subgroup of the Central Research and Development Committee in 1996, a group was set up with the remit of advising on how consumers could be involved in the R&D process. This set in train a series of publications and processes designed to achieve such involvement. As a result there is now a substantial literature reflecting on-the-ground experience of user involvement in the design and execution of clinical research.

Such involvement is also feasible elsewhere within the PPP. The House of Commons Health Committee (2002) review of NICE noted its proposals for improving the topic selection process, but went on to conclude that the proposals for widening participation still left the NHS – 'and in particular patients' – under-represented. It was offered evidence by NHS bodies that their perception of priorities was different from those of NICE but did not attempt to ascertain the views of patients directly in the course of its inquiry. NICE itself, however, has taken steps in this direction. For example, in support of its decision on the use of atypical anti-psychotics, NICE used reports by users on the side effects they experienced.

But it could go further. The evidence cited above taken by the Health Committee in the course of its investigation into NICE was based on a study of 40 patients with multiple sclerosis (MS) living in the London boroughs of Lambeth, Southwark and Lewisham. While NICE evaluated beta interferon, patients with MS surveyed by Lambeth, Southwark and Lewisham Health Authority expressed a desire for other forms of support – none sought more drug interventions (*see* House of Commons Health Committee 2002). The authority points out that the results are out-of-date, but suggests the (simple) process is a useful one.

The House of Commons Health Committee (2002, p 29) recommended that:

> *NICE should consider options for improving its evidence base in respect of patient experience and quality of life... and promote the routine inclusion of condition-specific quality of life measures into controlled clinical trials carried out prior to licensing by the pharmaceutical industry.*

In its response (Department of Health 2002e), NICE accepted the gist of this, as did the Government, which indicated that it was considering the role of the new Commission for Patient and Public Involvement in advising NICE on this issue.

Although these forms of user involvement are undoubtedly beneficial, they are tactical rather than strategic. The initiative lies mainly with the professionals, which is then modified by interaction with users. This fails to influence the much larger research budgets commanded by the private sector (into which the processes described above have not infiltrated). A strategic response involves assessing whether the care delivered is appropriate to the needs identified and whether the health research economy supports service change in the required direction. The evidence from the kind of work cited above and other studies suggests that neither is true.

A number of small-scale studies have been carried out to determine whether user preferences are the same as those of professionals. Such studies have generally found that user preferences do differ from those of professionals. A wide-ranging literature review carried out for the Department of Health (Grant-Pearce *et al* 1998) concluded that mismatches between professional/researcher and consumer groups were substantial, although they might change in the light of further information received by either 'side'.

A more recent study (Tallon *et al* 2000, p 2,039) identified what it described as a 'clear mismatch between the interventions that are researched and those regularly used and prioritised by consumers'.[54] They go on to point out that people use a range of treatment options, including many which are classified as complementary and alternative medicines (CAMs), but most studies focus on only some of them (usually drugs and surgical treatments). They conclude therefore that there is a need to 'broaden the research agenda to investigate whether other treatments are as effective as drug and surgical interventions'.

This mismatch reflects the key weakness in the patent system – its distortion of the 'playing field' for therapy development. How important it is in this context depends on the scope for interventions other than drugs. In the example taken by Tallon *et al* other options were available within the NHS – they were conventional rather than alternative treatments, but under-used. A recent survey of people with Parkinson's disease found that a substantial number had used alternative therapies, and, of these, 41 per cent found them 'of considerable benefit' (survey by the Parkinson's Disease Society reported in Melton 2003).

Studies of cancer patients show that a significant proportion back both horses. According to Morrell (2000):

> *Those people who are most likely to visit CAM therapists are generally those who are dissatisfied in some way with the conventional medical care they have received. That could be either through a longstanding problem being unresolved or through experiencing ADRs*

from a treatment. In both cases, the more articulate and intelligent patients, who are also generally the more assertive, will wish to try some new approach.

User support for CAMs – as revealed in surveys of this kind and through the use of such services – indicates in the clearest possible way that a significant number of people do not like conventional medicine or that it has failed them in particular ways. Evidence of this kind in other industries would lead to the inflow of new suppliers offering something different. Indeed, this is what has occurred in this sector in the United Kingdom and elsewhere: the number of CAMs practitioners has grown rapidly in recent years. The difficulty is that the health research economy has not developed so as to support changes of this kind for the reasons we have set out above. Although people may use chiropractors and find them beneficial, the research budget does not 'follow the patient' even though patient preferences are clearly demonstrated by the choices they make.

A redefined PPP would start from the presumption that, to a greater degree than now, the directions taken in the health research economy should be influenced by a fundamental perception of what people want and recognition that these wants may be diverse in terms of the therapies they would like to use, the type of relationship they want with a health professional and the extent to which they seek to make their own therapeutic decisions.

Work of the kind set out above sheds some light on these issues even if it is not targeted directly on them. Taking the (small) samples at face value suggests some users would prefer therapies other than those they are offered. But given the present nature of the NHS and the limited availability of evidence bearing on some therapeutic options, the scope for voting with one's feet in favour of alternative therapies or even comprehensive choice within mainstream therapies is limited. Those who are not currently choosing these options now may well consider doing so if the evidence base was there to support them. Therefore how people would choose if evidence of the effectiveness of all available options was pursued with equal vigour is an entirely open question.

We have briefly considered here a range of ways in which the interests of users could be better articulated within the process of drug (or therapy) development. The key question remains of how to give them effective purchasing power or enforce their preferences if, as with CAMs or low technology interventions such as exercise routines, these are of no interest to the pharmaceutical industry because they are not patentable. In technical terms the obvious route is through the current publicly financed research budget or through new schemes to encourage research in neglected areas of the kind already referred to. However, the main task is political rather than technical since it involves a potentially fundamental re-ordering of priorities based on a more radical analysis than has been attempted so far of what the NHS should provide.

The limited evidence available would suggest that if research monies were 'put to the vote' there would be substantial support for:

- treatments that individuals could apply to themselves
- treatments that did not involve invasive interventions
- measures that avoid the need for treatment
- drugs and therapies that could be shown to be low risk in terms of side effects.

Many conventional drugs and therapies meet these criteria as do other forms of therapy. However, the full potential of the alternatives may not be realised because the research support is relatively weak or because within the health care system as it stands the resources available for supplying them are very limited.

Role of the scientific and clinical professions

We have included science as a partner in the PPP on the ground that it is to a large degree self-regulating. But the evidence cited above suggests that in some instances it has been corrupted and to that extent it has not served the public interest. Some of the measures considered above such as greater transparency and more non-commercial funding for trials bear directly on this issue. The steps taken to counter the bias in publications by the medical and scientific press may also be helpful. But they may not be sufficient since the forces creating this bias are so strong.

Other measures are feasible. Quick (2001, p 776) argues that public–private partnerships must have 'a firewall (in principle an impermeable barrier) between the overall management of the project and the scientific evaluation of the results. The freedom to publish both positive and negative results is vital to the scientific integrity of such a partnership'. But the evidence cited here suggests that firewalls are hard to establish and maintain because of the pressure which is exerted on them. Within any one organisation a firewall might easily become porous. Accordingly, wider-ranging approaches are required, embodying the key element of this proposal which is independent and open evaluation.

Some of the criticisms set out above have found some response among policy-makers. This is particularly true of the governance of science where the Government and the scientific community itself have taken a number of measures designed to restore trust, largely through the involvement of lay people and greater openness about the advice that is offered. These measures have mainly focused on scientific advisory committees across government as a whole.

However, the arguments and evidence set out above on the conduct of science financed by the pharmaceutical industry suggests measures like these should be extended. We have noted in several places above the need for clearly independent scientific assessments, such as of ADR data. More fundamentally some of the key phases of drug development, in particular the conduct of trials, should be carried out or supervised by independent agencies.

Such independence cannot be achieved if the necessary institutions do not exist and/or if all those expert in particular fields are not actually or apparently independent. To achieve this requires much greater commitment of public resources supported by changes in the regulatory regime of the kind outlined above.

While funding is critical, it may not be enough on its own. Although we have focused here on the pressures exerted on science by the pharmaceutical industry, the health research economy suffers from biases of its own. The redirection of research so that it gives full weight to the user element of the PPP would find resistance on scientific grounds. This may well be justified but at times it will be spurious. Although science is essentially an open-minded activity, in the short term it often fails to be so. Orthodoxies are established and positions taken which can act as effectively as any economic monopoly to block new developments. The very processes which are designed to ensure the quality of scientific work, such as peer review, can act as a brake on new ideas.[55]

There is no complete 'answer' to this source of difficulty although a health research economy in which there is a variety of funders would be a partial solution. The United Kingdom already has a diverse research economy by virtue of its range of voluntary organisations supporting

research, but their resources are of course limited and in some cases their independence is more apparent than real.[56] There is a case therefore for promoting diversity (or at least providing the conditions for it) through long-term block – rather than project – funding and other measures designed to protect independence.

5 Recommendations and ways forward

This section sets out the recommendations of the paper under two headings: conceptual and practical. The main recommendation is that the Government should set up a Health Research and Development Task Force to systematically identify the areas that are poorly served by the current implicit public–private partnership (PPP). The section concludes by suggesting how the Government might approach this task and goes on to summarise current and planned work by the King's Fund in this area.

Our argument suggests the implicit PPP needs substantial modernisation. Two different approaches are required: the first conceptual and the second practical.

Conceptual recommendations

Although others have argued (*see*, for example, Whalley *et al* 2000 and Kay 2001) for an overall pharmaceutical policy for the United Kingdom that would bring together the various elements of government policy bearing on it, this call has not been answered. If our analysis is correct their call is, in any case, not correctly specified. What is in fact required is a therapeutic policy embracing all potential forms of health-promoting intervention, not just drugs. The core of such a policy would be to ensure that there was a level playing field between them as far as possible in terms of research funding, clinical trials and potential application. The notion of a level playing field is far from precise but at minimum it should mean that funding in the health research economy responds to evident shortfalls in particular areas, and that it embodies a process that takes an explicit view of the merits of different lines of investigation, not simply those which are commercially or scientifically attractive.

A further requirement is to consider all the elements of the PPP together. At present improvements are introduced piecemeal without regard for the context within which they operate. For example, the establishment of the National Institute for Clinical Excellence (NICE) represented a significant and (largely) desirable advance, but some of the difficulties faced by NICE – such as the lack of evidence or inability to access evidence – stem from weaknesses in other parts of the PPP, which NICE alone cannot remedy.

The *Science and Innovation Strategy* (2001a) published by the Department of Health is the closest the department has come to setting out its overall policy on knowledge generation, but this does not consider how the various elements interact, not only those within its own policies but also those of other departments. It does not systematically assess where the current system fails to deliver what the NHS needs. The same is true of the department's annual reports on the Pharmaceutical Price Regulation Scheme (PPRS). As a result, the existing implicit PPP falls short of what could be achieved. No mechanism exists to assess it as a whole.

The third requirement is for the customer side of the PPP to define what it wants, that is, to define an output specification which is precise enough to guide research into otherwise neglected areas, while not so precise as to preclude unconventional options. Thus a PPP focused on health would be based on the following key principles:

- ☑ Systematic evaluation of neglected areas of potential high benefit, whether in the development of new drugs/therapies or in areas such as post-licensing clinical trials. This could also be applied in areas such as back pain or stroke, which are highly expensive conditions but neglected in research terms and ignored by national priorities.

- ☑ Equality of opportunity for therapeutic options. Clearly there will be differences of expert view as to the merits of different lines of inquiry but the present situation is one in which some areas are neglected and will always remain so. Overcoming this will require new forms of intervention in the drugs/therapies development process that overcome the existing market failures, or modification of the public-sector research portfolio as proposed, for example, by the Medical Research Council in its clinical trials review (MRC 2003).

- ☑ All parts of the drug therapy development process should be considered at one and the same time. This includes the elements we have reviewed above as well as those we have not (such as NICE being considered as a single process). In other words, the requirements of effective decision-making should be given due weight.

- ☑ Citizens and service users should have a voice, based on surveys rather than representation, at all stages of the research process – the issues or problems to be researched, the kind of solutions to be considered and the actual design of the trials that ensue.

Practical recommendations

It has already been identified that some needs groups are neglected or poorly served by existing research and development programmes in the public and private sectors. There is therefore a case for a Health Research and Development (R&D) Task Force. This task force could set about systematically identifying all the areas poorly served by the current implicit PPP and identify the appropriate response on behalf of the Government, the rest of the public sector and the private sector.

This Health R&D Task Force should be established according to the following guiding principles:

- ☑ The task force itself should not directly involve any research providers. It should only include users of research such as clinicians and other decision-makers, and members of the public as actual or potential users of health services.

- ☑ Taking into account the principle above, its membership should be diverse in terms of disciplines and fields of expertise as well as personal experience.

- ☑ It should be able to commission research in its own right into public priorities and the current balance of research effort between new forms of treatment and other types of health care.
- ☑ It should operate on a continuing basis.
- ☑ It must be seen to be independent and therefore its operations need to be completely transparent.

Specific issues the Health R&D Task Force might consider include:

- how the public sector could be a better purchaser by developing the role of NiCE 'upstream' and ensuring that the earlier stages in the therapy development process produce the data it needs
- the gaps in the health research economy
- the economic advantages of alternatives to patents, which preserve incentives to drug development within the private sector
- how to redesign the process of defining the need for clinical trials so as to create a level playing field between trials driven by commercial interests and those undertaken for socially beneficial reasons
- how the process as a whole – not simply the individual parts – can be improved.

The recommendations set out above are intended to lead to the development of a public–private partnership (PPP) for the promotion of health. What the proposed Health R&D Task Force would in fact recommend remains an open question but it is likely that, at least in some respects, its proposals would conflict with the private sector's view of its own interests as creators of employment and other benefits to the UK economy. The Department of Health would therefore be faced with the tricky problem of how to put together the results of the work done by the proposed Health R&D Task Force and that of the Pharmaceutical Industry Competitiveness Task Force (PICTF).

It has to be recognised that if the department were to attempt this task it would face a fundamental difficulty: regulation of the pharmaceutical industry is an international enterprise and so there are limits to what one country can achieve on its own, particularly if, like the United Kingdom, that country has a substantial industry. But while this presents an obstacle to some possible policies, such as a substantial change in the licensing regime, it does not get in the way of others, such as a redirection or expansion of the funds currently devoted to health-related research.

Moreover, in this field, a greater degree of internationalisation would be a positive factor since all developed countries share similar problems around such issues as adherence to drug regimes and control of their drugs spending.[57] The recent report from the G10 (European Commission 2003) is an example of the scope for joint work. This report identifies a number of areas for international action but some, such as the creation of incentives to encourage research in line with public health priorities, can also be tackled at national level.[58]

The Department of Health has recently restructured itself so as to focus on the strategic issues that only it can tackle. The task of getting the best – from the health viewpoint – out of the UK pharmaceutical industry and the wider health research economy is surely one such issue.

Ways forward

The King's Fund is ready to support the establishment of a Health R&D Task Force, if others express an interest in its development. For this task force to be effective it must include the views of all those who may be poorly served by the existing arrangements. This means, primarily, the general public, who are current and/or future users of health care. It also means clinicians and public health experts who may challenge the focus of research programmes on new treatment as opposed to the effective application of existing interventions, or highlight bias towards commercially viable interventions over other approaches such as behavioural change or public health measures.

On a wider front, the King's Fund remains committed to improving health for all – and to challenging the inequalities faced by particular groups in society. Our activities include:

- **Promoting greater public and patient involvement in health and health care issues** – as a route to greater ownership of health and health issues at individual and community level, and to more responsive and inclusive services.

- **Drawing attention to areas where public interests, or the needs of particular communities, are under-represented** – such as the health-related research discussed in this paper, or the case for investing in local health 'advocates' in some of London's most deprived areas, to act as a bridge between health care professionals and their communities' needs.

- **Helping develop an effective health system** – with a greater focus on health outcomes, not simply on service delivery. In 2004, we launch a broad programme of work looking at how a complete 'health system' might work – for example, by building stronger leadership at national, regional and local levels, or developing local health organisations that help people safeguard and improve their health throughout their lives.

Endnotes

Section 1: An implicit public–private partnership

1 These other departments include the Department of Trade and Industry and the various funding bodies within the four countries of the UK responsible for higher education.

2 This is an updated version of Section VI of the task force's final report.

Section 2: The implicit PPP in outline

3 In fact, examples of state support for medical research can be found in the 19th century but on an *ad hoc* basis.

4 In this paper the term patents is used both for patents and for related legal forms that inhibit competition.

5 One department in each of the four countries comprising the UK.

6 The agency has recently merged with the Medical Devices Control Agency to form the Medical and Healthcare Products Regulatory Agency.

7 The case for public ownership was considered and rejected in the 1960s by the Sainsbury Committee. The committee was established to 'examine the relationship of the pharmaceutical industry of Great Britain and the National Health Service', but did not consider all the elements of the PPP.

8 In the case of health care, the introduction of the private finance initiative to hospital building required NHS purchasers to define output specifications for hospitals rather than the designs themselves. The intention – not realised in practice to any great extent as yet – was to encourage innovative ways of providing the outputs, that is, the services required by a hospital for its clinical work to be carried out effectively.

9 No similar figure is offered in relation to the health objective. Although the annual report on the Pharmaceutical Price Regulation Scheme from the Department of Health emphasises the economic strength of the industry, it makes no attempt to assess the value in health terms to UK residents of there being an industry in the United Kingdom. In official papers, there is either silence or the most perfunctory reference to the health benefits of an indigenous industry. This is all the more surprising since the international nature of the industry and of the knowledge on which it is based would suggest that the United Kingdom does not need an indigenous industry for the health benefits it brings. The drugs themselves and the results of clinical trials of their effectiveness are both transferable from one country to another. Countries without an indigenous industry simple import the pharmaceutical products they need.

10 *See*, for example, Cutler (1999) in respect of cardiovascular disease and for particular drugs, the numerous reports from NICE.

11 This does not imply that there have not been failures and disasters resulting from the introduction of drugs subsequently found to be dangerous.

Section 3: The elements of the implicit PPP

12 A small amount of direct funding comes from the Department of Trade and Industry.

13 *See* Rai (2001) and the references cited there.

14 In 1988 the House of Lords Science and Technology Committee published a report on medical research: for further discussion *see* Harrison and New (2002).

15 In contrast to those of the US National Institutes of Health, these UK public programmes are small: the overall UK public-sector budget plus the very considerable charitable trust contribution amounts to about one-third

of what the industry spends within the United Kingdom. However, like all other countries, it is a free rider on US publicly financed research that raises the question of what a specifically UK contribution should be. As far as the author is aware, that question has not been addressed in any paper published by the Department of Health.

16 This point is argued in detail in Harrison and New (2002).

17 These conclusions were criticised by a number of commentators on the original article. However, the basic point that the new drugs are very expensive was not refuted.

18 *The Financial Times* has frequently reported on the lack of new products emerging from the industry.

19 This statement appears to be in strong conflict with other work which suggests that the returns from medical research are very high indeed (*see*, for example, Murphy and Topel 2003). One possible explanation is that returns in the past were high but that prospective returns are now much lower.

20 It is one of the curiosities of officially inspired research reviews that they omit the worldwide health research economy in the areas they review, including both its public and private components.

21 The pharmaceutical industry is, however, particularly dependent on patents (*see* Kay 2003).

22 The United States passed the Orphan Drug Act in 1983. While it has encouraged development of drugs for rare conditions, it has had other less desirable impacts (*see* Maeder 2003).

23 The privatisation of knowledge of particular genes has been a source of particular concern. A related problem arises where companies possess patents which they do not exploit for commercial reasons but which they do not allow others access to.

24 The Royal Society (2003, para 3.5) has recently expressed concern over the scale of this form of privatisation. Its report points out that 'only by having knowledge unencumbered by property rights can the scientific community disseminate information and take science forward'. It also points out that the open source software movement – a kind of anti-patent movement – is proving successful.

25 *See*, for example, Trouiller *et al* (2002).

26 Despite the confidence of the Medicines Control Agency (MCA), the Committee on Safety of Medicines issued a warning on the use of Seroxat for the treatment of children with depression in June 2003 (Department of Health 2003c).

27 In 1997 the US Government passed the Food and Drug Modernisation Act which provides for a financial incentive by way of a six-month extension on the patent for medicines. It has resulted in more clinical trials involving children but not, according to Choonara (2000), where the greatest need is.

28 *See* Harrison and New (2002) for further examples.

29 In fact there has been publicly funded research in this area.

30 This gap was identified in a report from the House of Lords Science and Technology Committee in 1988; for further details *see* Harrison and New (2002).

31 Garattini *et al* (2003) note that: 'In recent years superiority trials have often been replaced by equivalence or non-inferiority trials'. They argue that this switch is unethical for a number of reasons and hence that such trials are not in the patient's interest – even if they are in the commercial interests of the companies sponsoring them. Accordingly, they urge research ethics committees to protect patients from such trials which offer little or no potential benefit at some potential cost. For further discussion *see* Ellenberg and Temple (2000).

32 In 2000 the health care panel of the Foresight Programme called for a national strategy for clinical trials and the establishment of NHS Enterprises to handle all aspects of the interface with the private sector. This call has not been answered.

33 *See*, for example, Mundy (2001) and Moore (1989).

34 The Medicines Control Agency has merged with the Medical Devices Agency to form the Medicines and Healthcare Products Regulatory Agency (MHRA).

35 *See also* Horton (2003) for data on the negative effects of licensed drugs.

36 The House of Commons Health Committee also took the view that the competing interests of health and wealth did not sit well together within the same organisation. The Government responded to this argument by creating a division within the Department of Health between industry and other interests. Since then, the agreement has been renewed to the apparent satisfaction of both sides.

37 Recent NICE decisions have been criticised precisely for this reason, particularly as the Government has required the NHS to abide by them.

38 However, Hughes *et al* (2002) have attempted to measure this. They conclude there is a case for extending patent life/high prices on the ground that the future gains of doing so outweigh the immediate benefits of lower drug prices.

39 Maynard and McDaid (2003) point out that economists too have 'deviated to comply with industry's commercial goals.'

40 In 2002 the director of the Division of Cellular and Gene Therapies at the Food and Drug Administration (FDA) stated that he thought that the 'credibility of clinical research in the US had been severely damaged in part because of a failure to fully inform the public about the involvement of participants in clinical trial' (*see* Marwick 2002). A recent issue of the *British Medical Journal* (2003, vol 326) contained several articles bearing on the issues considered in this section, but from the viewpoint of the medical profession.

41 For a discussion of what 'disentanglement' would mean for the medical profession *see* Moynihan (2003a, 2003b).

42 We noted above that Gale recommended these; he is just one author of many following the same logic to the same conclusion.

43 *See* Harrison and New (2002) for further discussion.

Section 4: Widening the public–private partnership

44 *See* Sobel (1996).

45 For more examples of the use of rewards in recent times, *see* Shavell and van Ypersele 2001.

46 *See* Sudlow and Counsell (2003). They make the point that the process ignores a cheaper alternative, something an informed purchaser would not have allowed. For a more positive view, *see* Chapman *et al* (2003).

47 This was part of the Department of Trade and Industry's LINK programme, which contained a number of programmes bearing on health (*see* www.healthtechnologyportal.org.uk for information on current programmes of support).

48 In the world of information technology, the obvious parallel is the development of Linux as an alternative to Microsoft products.

49 For further discussion *see* Chapter 2 of Harrison and New (2002). *See* also Al-Shahi *et al* (2001) who found that researcher interest in rare conditions was disproportionately larger than their interest in common conditions.

50 This point is discussed in Chapter 6 of Harrison and New (2002).

51 *See* Folkers and Fauci (1998) for a review of similar developments in the United States.

52 A number of US studies suggest the returns are very high when measured in terms of extra life expectancy (*see*, for example, Murphy and Topel 2003).

53 The Consumers' Advisory Group for Clinical Trials was established in 1994 to promote patient involvement in trial design.

54 The work described by Tallon (2000) and colleagues has the immense advantage of embodying the views of (relatively) large numbers of people, which representation cannot do.

55 *See* Harrison and New (2002) for further discussion of this point.

56 In some cases these bodies are dominated by existing scientific interests.

Section 5: Recommendations and ways forward

57 *See* WHO (2003).

58 The press notice accompanying this report is headed 'Commission pushes for a stronger European-based pharmaceutical industry for the benefit of the patient', thus mirroring the blurring of patient and industrial health interests apparent in statements from the Department of Health.

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